Agmaset® and AgmaVet® Science Leading to Product



Agmaceuticals®:

Nutraceuticals containing the neuroprotective ingredient G-Agmatine®.

G-Agmatine® The best brand of agmatine.

https://ForNerveHealth.com

Neuroscientists - 1977

<u>Donated to</u> – Dr. Donald J. Reis's

Laboratory of Neurobiology, Cornell

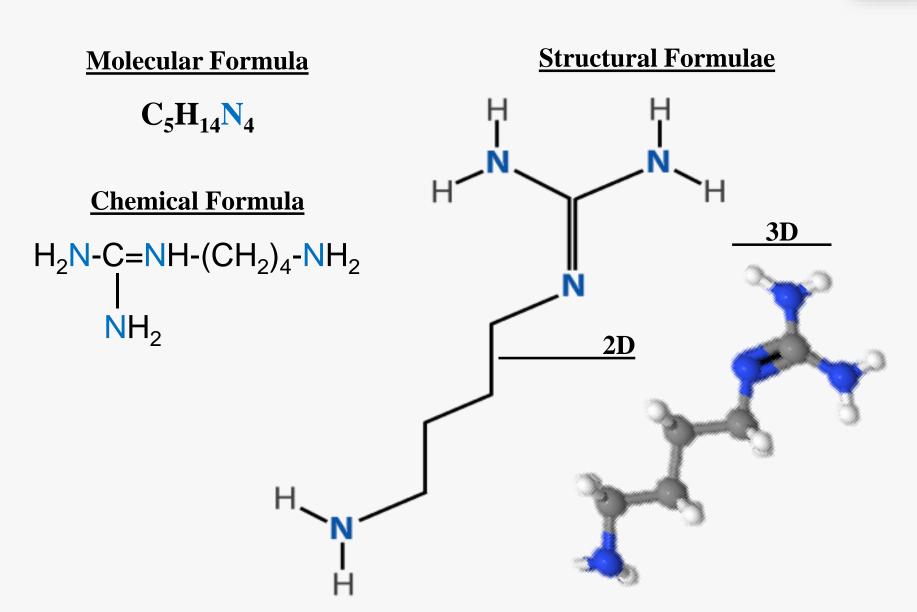
University Medical College.

(oil pastel on paper)



Agmatine

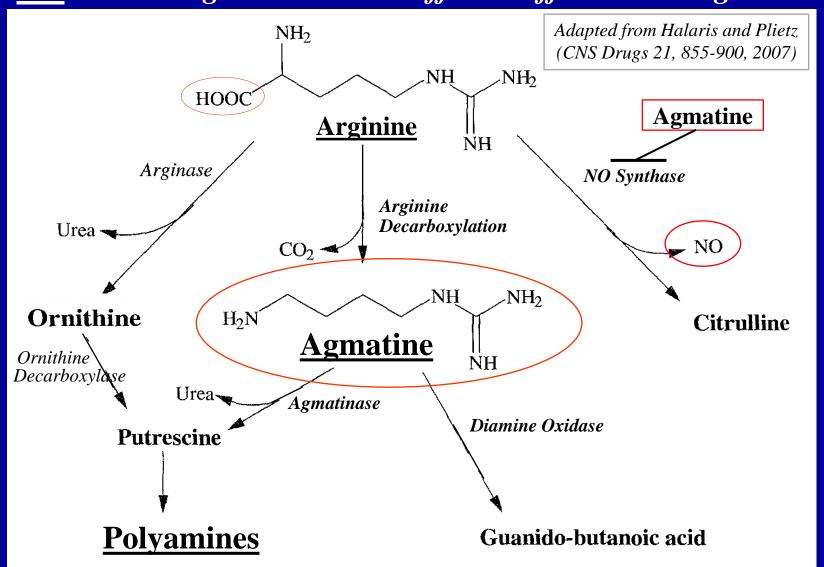




Metabolic Pathways



-Agmatine is a metabolite of the amino acid arginineBut the base agmatine exerts different effects than arginine





Agmatine is a Naturally Occurring Compound with Broad Distribution in the Body

• Brain: 300 ng/mg

• Blood: 47 ng/ml

• Intestine: 55 ng/mg

• Fecal: 3,290 ng/g



Agmatine is a Ubiquitous Compound Present in Many Plant- and Animal-Derived Foodstuff

- Commonly found in foodstuff derived from plants, fish and animals (usual range: 0.1 10 mg/kg).
- High levels are found in certain fish products (200 and up to 650 mg/kg).
- Intestinal microbial production is considered a major source of agmatine.

Agmatine May Exerts Multiple Effects-Animal Model Experiments-



- Neuroprotection.
- Healthy pain-free nerve functions.
- Healthy mood functions.
- Healthy coping with Stress.
- Learning and memory enhancement.
- Healthy blood glucose regulation.
- Healthy blood flow.
- Protection of healthy kidney functions.
- Healthy control of cell growth.

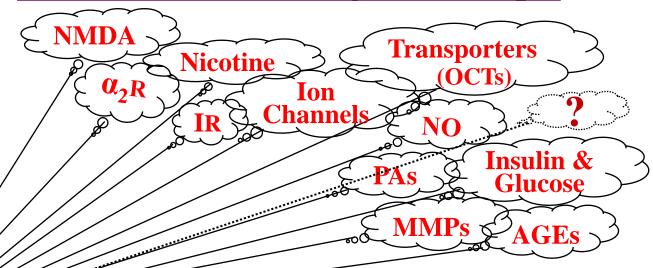
UNIQUE MECHANISM OF ACTION





Firing Squad
(Polypharmacy)

'The Molecular Shotgun Concept'



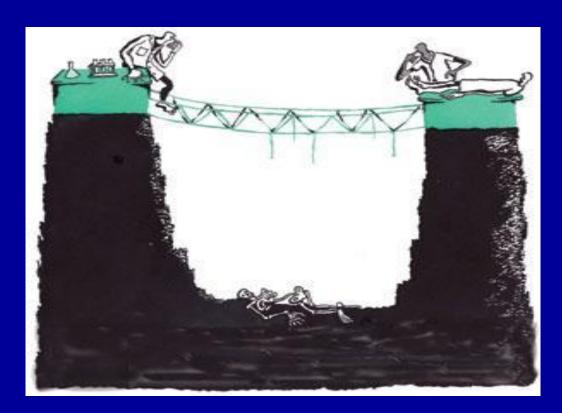


Agmatine Modulates Multiple Molecular Targets



Translating Research Into Practice

'The Valley of Death'
Where some 99% of treatments fail





Human Studies

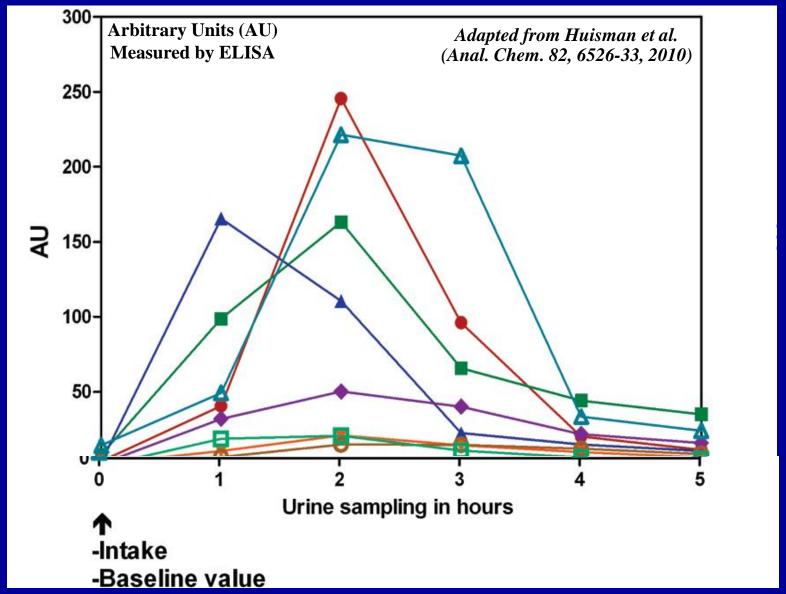


Absorption, Distribution, Metabolism and Elimination

- Oral agmatine is absorbed by the gastrointestinal tract.
- Agmatine is distributed throughout the body. It crosses the blood-brain-barrier (animal studies).
- Agmatine is mostly converted to putrescine, precursor for polyamine synthesis, and urea. Some may be oxidized.
- Agmatine is excreted by the kidneys.

Agmatine in Urine Following Oral Intake (2 hr apparent blood half-life)







Addressed Conditions

Approximately 30 million people in the United States alone cope everyday with circumstances that challenge healthy nerve functions...

Safety Clinical Trial



-Open Label, Dose-Escalating Clinical Study Design-

Keynan et al., Pain Med., 2010;11(3):356-368

Cohort	Participa [Male] [Fe		Treatment Regimen
1st Cohort	[3]	[2]	1 capsule 3 times daily (1.335 g G-Agmatine/day) - 10 day treatment
2 nd Cohort	[1]	[4]	2 capsules 3 times daily (2.670 g/day) - 10 day treatment
3 rd Cohort	[7]	[5]	8 daily capsules (2 in the morning, 3 at noontime and 3 in the evening) (3.560 g/day) - 10 day treatment
4 th Cohort	[8]	[4]	8 daily capsules (2 in the morning, 3 at noontime and 3 in the evening) (3.560 g/day) - 21 day treatment

Adverse Effects During 7-month Follow-up	1st Cohort	2 nd Cohort	3 rd Cohort	4 th Cohort
Mild Diarrhea			1	2
Discontinuations – Due to the above Adverse Effects				1
Free Will Discontinuations				1

Long-Term Safety

-A Case Report-



Gilad and Gilad, J. Medicinal Food, 2014;17 (11):1–4

Regimen: The recommended daily dose of 2.67 g oral G-Agmatine® was taken over a period of 4–5 years. The regimen consisted of six gelatin capsules, each containing 445 mg, taken twice daily three in the morning and three in the evening after meals.

Measures: Clinical follow-up consisted of periodic physical examinations and laboratory blood and urine analyses.

Results: All measurements remained within normal values and good general health status sustained throughout the study period, up to 5 years.

The studies provide evidence for the long-term safety of a high daily dosage of G-Agmatine®, and indicate that it is non-addictive.

Translation of Research into Treatment Fight For Nerve Health



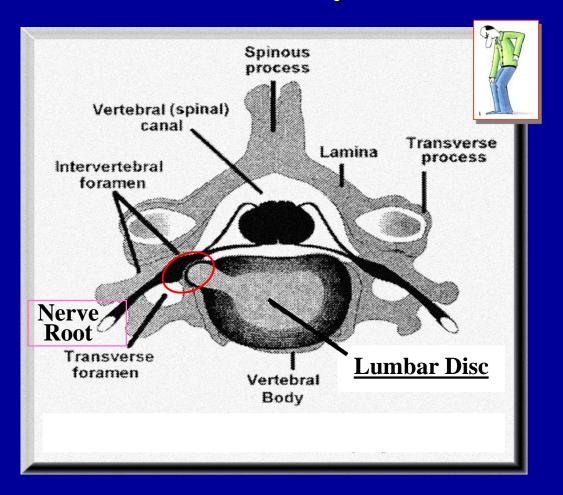
-Clinical Study Focused on Sciatic Nerve-



Clinical Study



- ➤ About 1.5% of the population cope everyday with circumstances that challenge healthy sciatic nerve functions.
- > Sciatic nerve functions can be clearly defined and measured.



Efficacy Study — Sciatic Nerve Functions

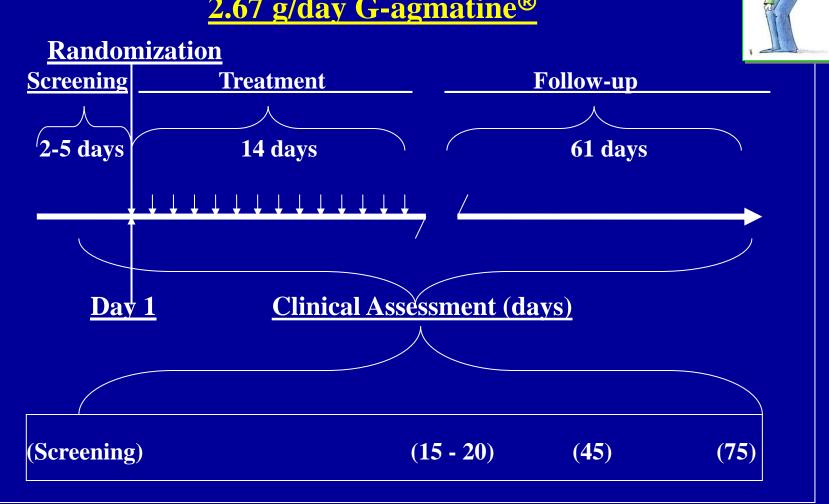


Randomized, Double-Blind, Placebo-Controlled Trial (RCT)

Keynan et al., *Pain Med.*, 2010;11(3):356–368

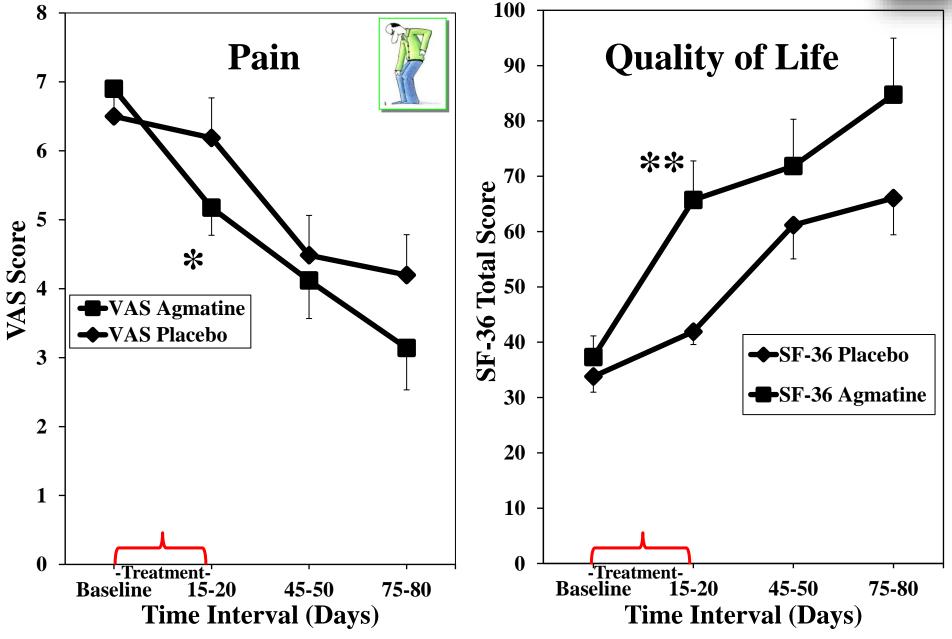
-Study Design-





Efficacy of G-Agmatine®







Effectiveness in Small Nerve Fiber-Associated Pain

Open-Label Consecutive Case Series Study

Rosenberg et al., Nutrients, 2020;12(2):576

> Small fiber nerve malfunctions underlie symptoms associated with various types of bodily systems disorders

Pain questionnaire ratings before and after 60-day treatment with G-Agmatine®

Stud Patientsen- 2 (11)	Ayerage Pain .67 B <mark>efore</mark> -agn	Ayerage Pain latineAffer 60 da	Absolute <mark>VS</mark> Decrease	Percent
(11)	Treatment	Treatment	(Rating Points)	Decrease
Average ± SD	56.1 ± 18.2	30.1 ± 16.9	26.0 *	46.4% *

^{*}Highly significant (p < 0.00001, paired t-test). SD, standard deviation.



"Proof-of-concept"

The human clinical studies serve
a "Proof-of-concept" indicating the
safety and effectiveness of G-agmatine®
treatment for healthy nerve functions
under stressful conditions



Recommended Effective Regimen

- > 2 to 3 capsules twice a day with or after meals for as-long-as needed (each capsule contains 445mg of *G-Agmatine*®).
- > Time to effect -
 - In acute circumstances: 2 4 days in most, but may be as-long-as 2 to 4 weeks.
 - Chronic conditions: 3 6 weeks.
- After the effect is established dosage may be gradually reduced for maintenance regimen.



AgmaSet® First-of-its-Kind Dietary Supplement Containing G-Agmatine® For Nervous System Health and Proper Nerve Functions

For Healthy Nerve Functions*

DIRECTIONS FOR USE: Adults, 2 capsules twice or three-times a day with or after meals, or as recommended by your physician, pharmacist or healthcare professional.

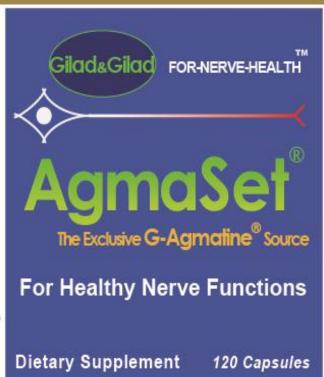
NOTE - Pregnant or nursing women, children and III or medication-taking people should consult a physician befor use. May cause diarrhea.

- Keep Out of the Reach of Children.
- Do Not Use If Printed Seal is Broken or Missing
- Store in a Closed Bottle at Temperature Not Exceeding 30°C (86°F) and Humidity Not Above 70% RH.

*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.



Gilad & Gilad LLC
Henderson, NV 89015. Tel: 1-888-484-4523
Info@ForNerveHealth.com
www.ForNerveHealth.com



Supplement Facts

Serving Size: 2 Capsules Servings per Container: 60

Amount per Serving		% Daily Value	
Calories:	less than 1		
Agmatine Sulfate (as G-Agmatine®)	890 mg	t	

TDaily Value Not Established

Other Ingredients: Gelatin, titanium dioxide (as capsule color), water. No allergens, preservatives or additives. Gluten-Free. Each bottle contains one (1) nontoxic desiccant packet. G-Agmatine® is a trademark brand of Gilad&Gilad LLC. Patents U.S. 8,916,612; U.S. 9,585,852.

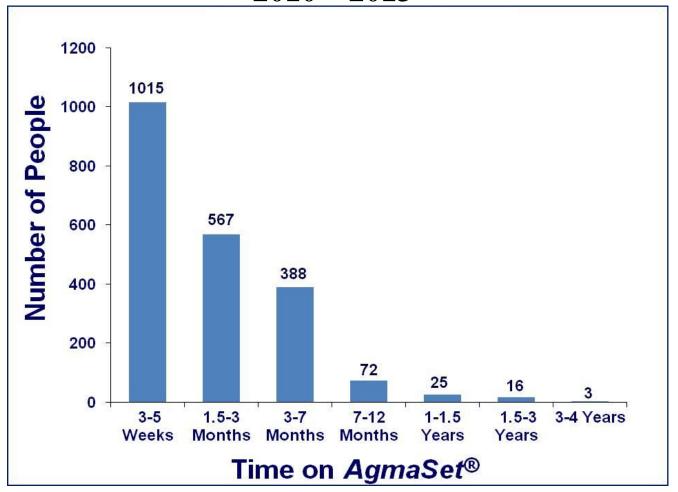
MADE IN THE

USA



Safety and Effectiveness of *AgmaSet*® 2010 – 2013*





*Surveillance of people who took AgmaSet® during the years 2010 and 2013.

-No adverse effects were reported. -Three people reported soft stool or mild diarrhea.



Animal Studies

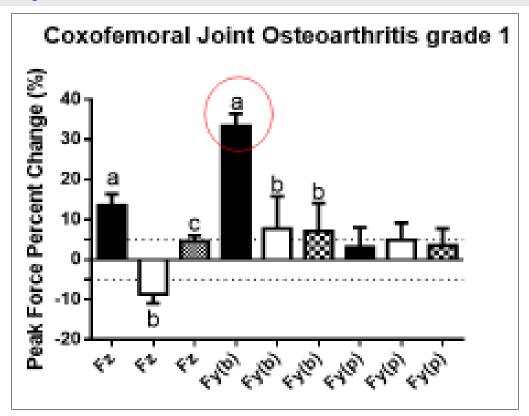


Effectiveness in Dog Hip Joint-Associated Symptoms



-A Randomized, placebo-controlled, crossover design-

Taguchi et al., Frontiers Vet. Med., 2018; 5, Article 311



Peak force percent change (mean +/- SEM) in dogs with grade 1 coxofemoral (hip) joint osteoarthritis following treatment with agmatine (black bars), placebo (white bars), or carprofen (gray bars). Fz, vertical force; Fy(b), braking force; Fy(p), propulsion force. Letters indicate significant differences among treatment groups (p < 0.05). Dashed horizontal lines demarcate 5% positive (upper) or negative (lower) changes.

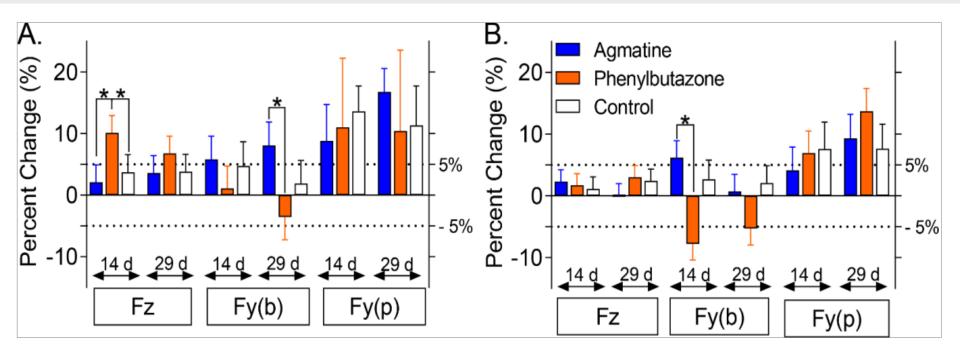


Effectiveness in Horse Lameness and Gastric Ulceration



-A Randomized, placebo-controlled, crossover design-

Taguchi et al., J. Clin. Med., 2022; 11, 7283



Percent change in lameness scale (LS mean \pm SEM) in thoracic limb ground reaction forces over the baseline. Peak force (A) and impulse (B) in vertical (Fz) and craniocaudal braking (Fy(b)) and propulsion (Fy(p)) after 14 and 29 days of oral agmatine (blue), phenylbutazone (orange), or control (white) administration. Asterisks indicate differences among treatments within time points (p < 0.05). A 5% change from the baseline (dotted lines) is indicated.

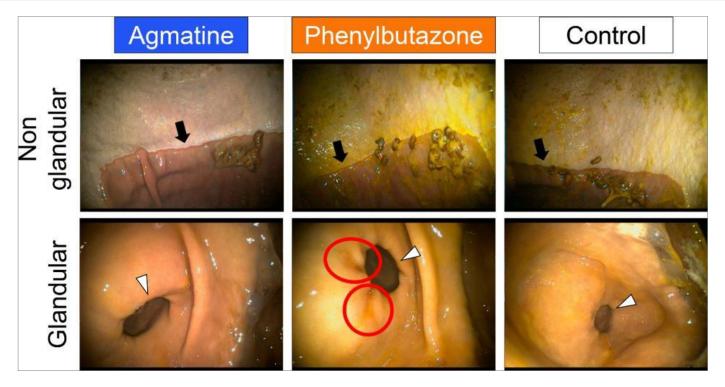




Effectiveness in Horse Lameness and Gastric Ulceration

-A Randomized, placebo-controlled, crossover design-

Taguchi et al., J. Clin. Med., 2022; 11, 7283



Representative gastroscopic images of equine non-glandular and glandular gastric mucosa after 30 days of oral agmatine (**left**), phenylbutazone (**middle**) or control (**right**) administration. Ulcers in the glandular region are indicated with red circles. The margo plicatus (black arrows) and pylorus (white arrowheads) are also visible.

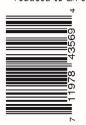


$AgmaVet^{\mathbb{R}}$ For Your Animal's Daily Diet Containing G-Agmatine® For Nerve Health

For Healthy Nerve Functions

Directions for use:

Adult animals - Recommended administration is 1 to 3 capsules a day (depending on body weight) with or after meals. Initial administration period is 4 to 6 weeks; however, some animals may respond in a shorter time period. The number of capsules may then be gradually reduced to an effective maintenance level.



Note - For pregnant or nursing females, young ones or ill and medication-taking animals, consult a veterinarian or health professional before use. May cause diarrhea.

Visit www.ForNerveHealth.com



Gilad&Gilad LLC Henderson, NV 89015. Tel: 1-888-484-4523 info@ForNerveHealth.com www.ForNerveHealth.com



120 Capsules

Each Capsule Contains:

Agmatine Sulfate (as G-Agmatine®).......445 mg*

Other Ingredients: Gelatin, titanium dioxide (as capsule color), water.

No allergens, preservatives or additives. Gluten-Free.

Each bottle contains one (1) nontoxic desiccant packet.

*Not recognized by the AAFCO as an essential animal nutrient.

G-Agmatine is a trademark brand of Gilad&Gilad LLC. Patents U.S. 8,916,612; U.S. 9,585,852.

- Keep out of the reach of children.Do Not Use If Printed Seal is Broken or Missing
- Store in a Closed Bottle at Temperature Not Exceeding 30°C (86°F) and Humidity Not Above 70% RH.

MADE IN THE

USA





Alternative Agmatine Sulfate-Containing Products

- ➤ All alternative products containing agmatine sulfate are based on borrowed science. All clinical studies are borrowed from Gilad&Gilad.
- ➤ Products targeting the bodybuilding field are all touted based on scientifically unsubstantiated claims and often on downright erroneous scientific information.
 - ❖ No evidence for enhanced Growth Hormone functions.
 - Agmatine may modulate Nitric Oxide (NO) synthesis, but does not enhance NO content.
 - * No evidence for enhanced muscle protein synthesis.

THANK YOU! PLEASE SPREAD THE GOOD NEWS





Any Questions?

Call us: (toll-free) 1-888-484-4523, or 1-702-790-2877

Contact us via email: <u>info@ForNerveHealth.com</u>

https://ForNerveHealth.com