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GedaCure[®]

crisdesalazine



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Canine cognitive dysfunction syndrome, CCDS

Canine cognitive dysfunction syndrome (CCDS) is a degenerative brain disease in senior dogs which is characterized by clinical signs related to behavioral alterations. The CCDS is also known as canine dementia and shows very similar characteristics to Alzheimer's disease (AD). CCDS and AD occurs due to the brain cell death caused by accumulation of amyloid plaque, phosphorylation of tau protein, excessive oxidative stress, and inflammation.

Dogs with CCDS show various clinical signs associated with behavioral changes, and the following acronym **DISHA**¹ describes the most common signs of CCDS.

- ✓ Wandering aimlessly or entering a corner and failing to return.

"Once, he ran into the wall and injured his nose. I'm afraid he'll harm himself again if I leave him alone."

Lee, OO
: Owner of "Jjong-i (Welsh corgi, 17-yr-old)"

- ✓ Activity level or interest in playing decreased.

- ✓ Urinating or defecating in the house.

"My dog would poop anywhere in the house and will step on it which he ends up leaving foot marks with his poop. It takes all day to clean after him"

Jung, OO
: Owner of "Jjang-a (Chihuahua, 16-yr-old)"

- ✓ Changes in Interactions with the family, other animals or people

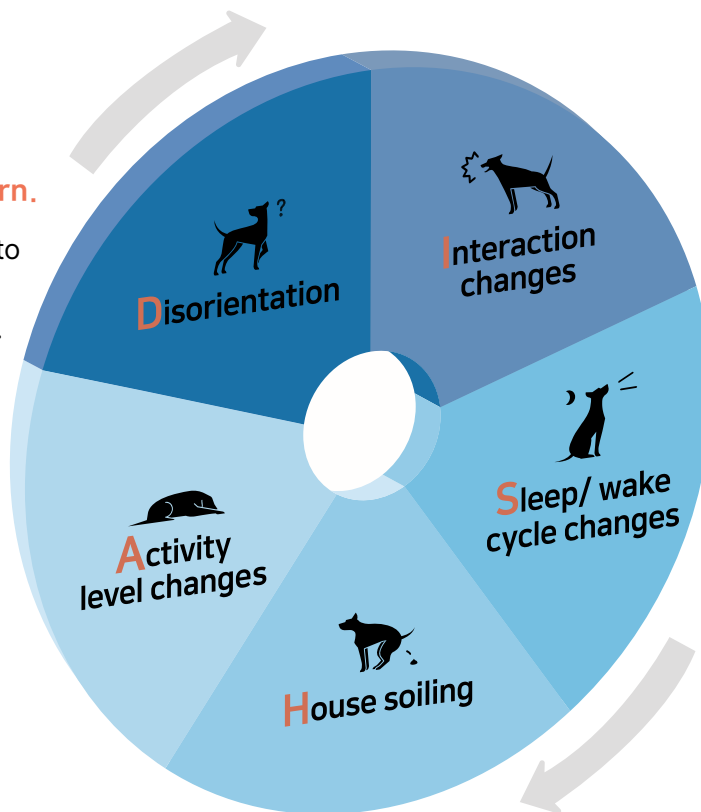
"She growls whenever I try to hug her and it makes my heart break."

Park, OO
: Owner of "Yang-cho (Mongrel, about 12-yr-old)"

- ✓ Changing in sleep patterns or a disruption of circadian rhythms.

"My parents can't sleep because my dog would bark all night, so I even considered euthanasia."

Lee, OO: Owner of "Bok Sil-I (Maltese, 13-yr-old)"



You can easily check symptoms of CCDS on the web site!

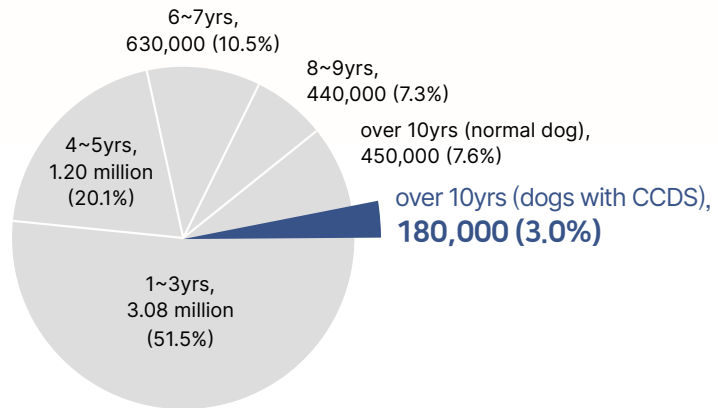
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Senior dog population in South Korea



About 28% of 11~12-year-old dogs and 68% of 15~16-year-old dogs are diagnosed with CCDS².

Thus, it is estimated that more than **180,000 of the 5.98 million dogs in South Korea are suffering from CCDS^{3,4}**. Furthermore, the number of dogs with CCDS are expected to increase steadily in the future as the life span of dogs are increasing.



<Proportion of dogs by age and estimated number of dogs with CCDS in South Korea^{2,3,4} (2019)>

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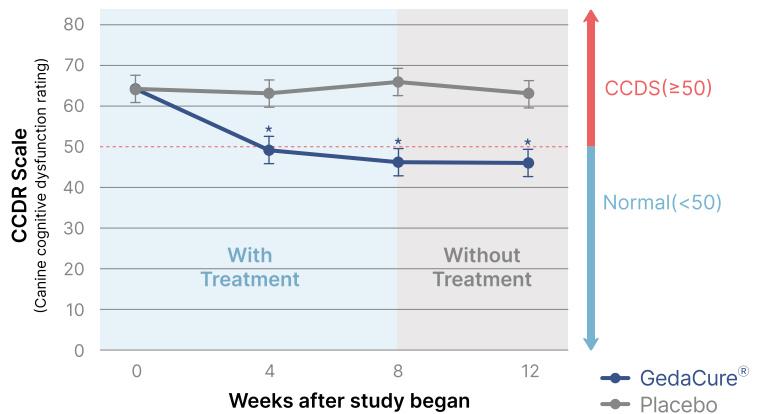
Effects of GedaCure[®]: CCDS⁵ questionnaire



Canine Cognitive Dysfunction Rating (CCDR) is a common questionnaire for diagnosis of CCDS all over the world. If the score on the CCDR is more than 50, dogs can be diagnosed with CCDS.

After 8 weeks of GedaCure[®] treatment, the CCDR score significantly decreased. Compared to the deterioration of the CCDR score in the placebo group, GedaCure[®] shows an excellent therapeutic effect.

In addition, the therapeutic effect of GedaCure[®] remained about 3 months after the usage of the medication. These results show that GedaCure[®] not only has a symptomatic effect, but **also has a disease-modifying effect through fundamental disease control**.



<The results of the clinical study conducted at the College of Veterinary Medicine of Seoul National University and 5 animal hospitals in South Korea>

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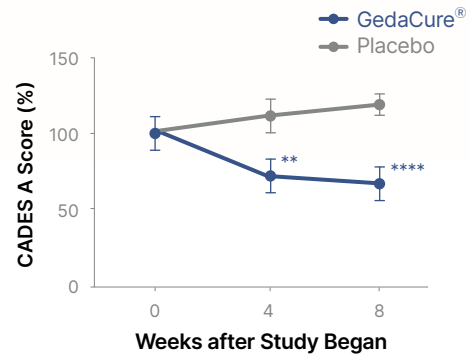
Effects of GedaCure[®] : CADES⁶ questionnaire

As with CCDR, the Canine Dementia Scale (CADES) is a worldwide CCDS diagnostic questionnaire. The CADES consists of four categories: spatial orientation, social interaction, sleep/wake cycles, and house soiling. Dogs with CCDS that took GedaCure[®] showed significant behavioral improvements for all categories in the CADES questionnaire.



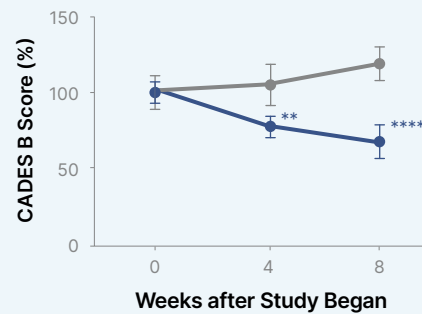
Improvement of spatial orientation

GedaCure[®] prevents dangerous situations such as dogs banging into the wall and being trapped under the furniture.



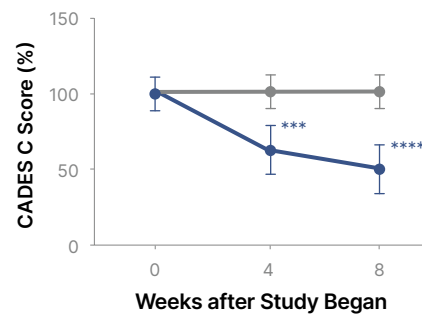
Increase of social interaction

GedaCure[®] improves social and emotional interaction between the dog and the owner.



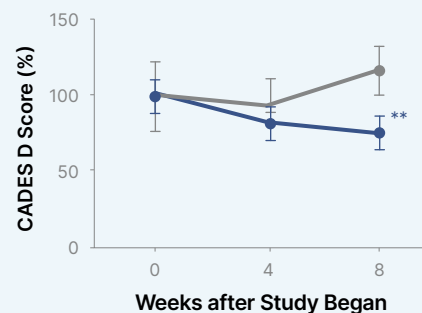
Improvement of sleep/wake cycles

GedaCure[®] provides a comfortable night to the owner and the dog who has suffered from insomnia.



Improvement of house soiling

GedaCure[®] releases the concern of the owner who is suffering from hygiene problems.



<The results of the clinical study conducted at the College of Veterinary Medicine of Seoul National University and 5 animal hospitals in South Korea.>

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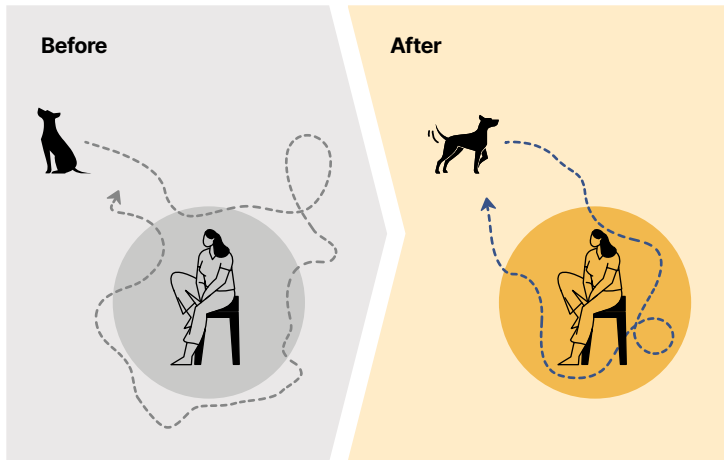
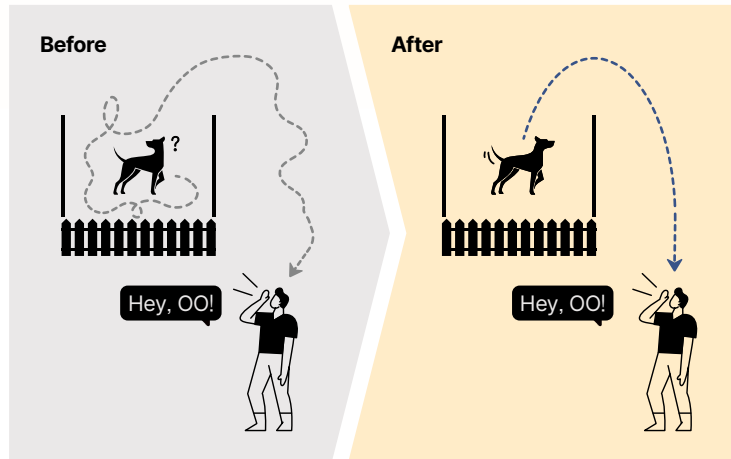
Effects of GedaCure[®] : Behavioral Functional Test



✓ Improvements of spatial & obstacle perceptual capabilities

In the cases of the dog with CCDS that took GedaCure[®] showed improvements in spatial and obstacle perceptual capabilities by distinctly shortening the the time to get out of the fence compared to the dogs that took placebo.

* "Get out of the wall" test: We timed how long it took for the dog to get out of the U-shaped fence when called by the owner.



✓ Improvement of social interaction

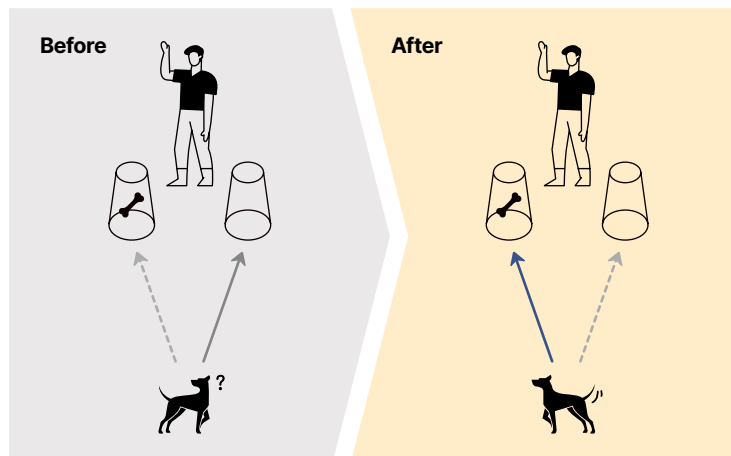
Dogs with CCDS that had reduced social interaction skills rarely stayed around their owners. However, after taking GedaCure[®], the dogs stayed with their owners for a longer time.

* "Social interaction" test: We measured the amount of time when a dog and its owner are together in a designated space.

✓ Improvement of memory loss

The significant increase in the number of successes indicates that GedaCure[®] improves visual short-term memory and training ability with rewards.

* "Find hidden food in a cup" test: After putting two cups upside down, we hid a treat in one of the cups. We counted the number of times the dog has succeeded in finding it.

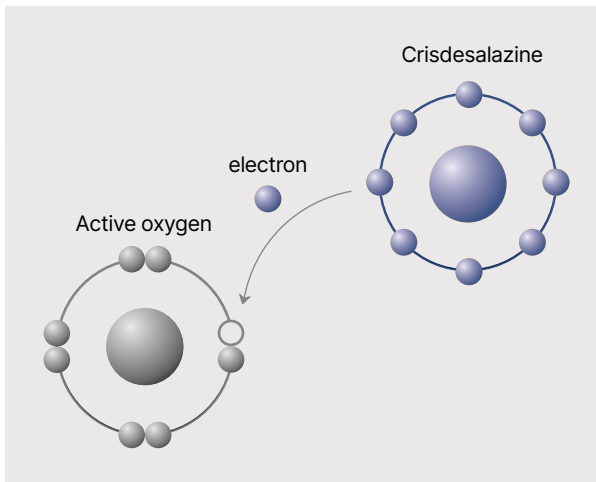


<The results of the clinical study conducted at the College of Veterinary Medicine of Seoul National University and 5 animal hospitals in South Korea.>

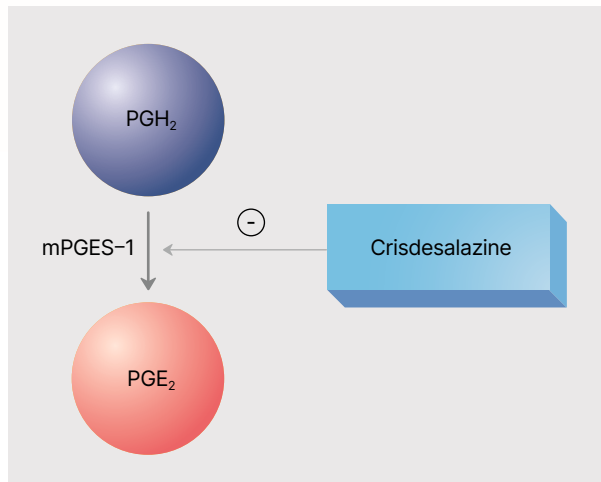
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Crisdesalazine : Multi-Target Neuroprotectant

Crisdesalazine, the active ingredient of GedaCure®, is a new drug with dual pharmacological mechanisms acting as powerful antioxidant action and anti-inflammatory action. It has been proven that cridesalazine improves cognitive function by effectively preventing both oxidative stress and inflammation in the brain, leading to protecting neurons in transgenic mouse models of Alzheimer's disease⁷.



» Cridesalazine reduces oxidative stress in neuronal cells by removing hydroxyl radicals.

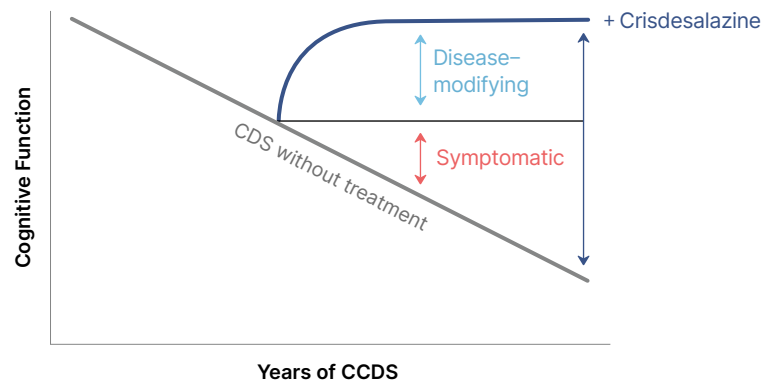


» Cridesalazine is an mPGES-1 inhibitor that reduces inflammation in the brain by inhibiting PGE2 synthesis.

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Crisdesalazine : Symptomatic & Disease-modifying effects

Symptomatic effect is the effect of alleviating the clinical symptoms caused by the disease. On the other hand, the disease-modifying effect is the effect of fundamentally treating the disease and returning the dog to its normal state. Until now, drugs used in canine cognitive dysfunction syndrome do not provide a fundamental treatment for the disease because they only have the symptomatic effect. However, cridesalazine has a disease-modifying effect as well as symptomatic effect, so it enables fundamental treatment of CCDS.



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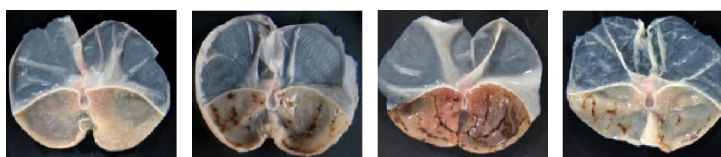
Crisdesalazine : Safety

After the oral administration of crisdesalazine once daily at 200 mg/kg which is 40 times higher than the recommended dose in dogs for 13 weeks, no significant differences were observed between the dogs treated with crisdesalazine and the normal control group dogs treated with its vehicle in vital signs (blood pressure, heart rate, etc.), electrocardiogram, ophthalmic examination, complete blood cell count, serum chemistry, urinalysis, and the histological examination of other organs.

Additionally, no significant abnormal findings were observed after the administration of crisdesalazine in our phase III clinical trial for marketing approval when the above examinations were conducted for dogs with cognitive dysfunction syndrome.



We compared the gastrointestinal side effects of crisdesalazine and several commonly prescribed, representative NSAIDs (Non-Steroidal Anti-inflammatory Agents) after the oral administration at high doses in rats. The rats treated with aspirin, ibuprofen, or celecoxib showed significant gastrointestinal bleeding, whereas the other rats treated with crisdesalazine did not induce any gastrointestinal side effects even at 1000 mg/kg dose that is 200 times higher than the recommended dose.



Crisdesalazine
1000mg/kg

Aspirin
300mg/kg

Ibuprofen
300 mg/kg

Celecoxib
1000 mg/kg

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GNT Animal Health

GNT Pharma is a company that strives to discover and develop new innovative drug candidates for patients who are suffering from neurological brain disorders and their families due to the lack of effective treatment. GNT Animal Health Business Unit has made every effort to apply our Alzheimer's disease drug candidate for CCDS treatment. And for the first time in South Korea, 'GedaCure®' has been approved as a drug for CCDS.

GedaCure®

crisdesalazine

Dogs change as they get older.
Owners feel sorry for the change,
blame themselves, and get tired.

Protect the happiness of the dog and the owner
with GedaCure®.

Product				
Product Name	GedaCure chewable tablet S (10 mg)	GedaCure chewable tablet SM (20 mg)	GedaCure chewable tablet M (40 mg)	GedaCure chewable tablet L (80 mg)

Dosage	Weight(kg)	Number of tablet per day			
	1.5 to 2.9	1 tablet			
3 to 5.9		1 tablet			
6 to 11.9			1 tablet		
12 to 24				1 tablet	
Administer orally according to the dog's weight as above. (3.3 – 6.7 mg/kg)					

Reference

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Telephone | +82-70-7725-9838
E-mail | gntanimalhealth@gntpharma.com
Address | 23, Yonggu-daero 1855beon-gil, Giheung-gu, Yougin-si, Gyeonggi-do, 17096, Republic of Korea
Website | www.gnt-animal-health.com