CALMING SUPPORT

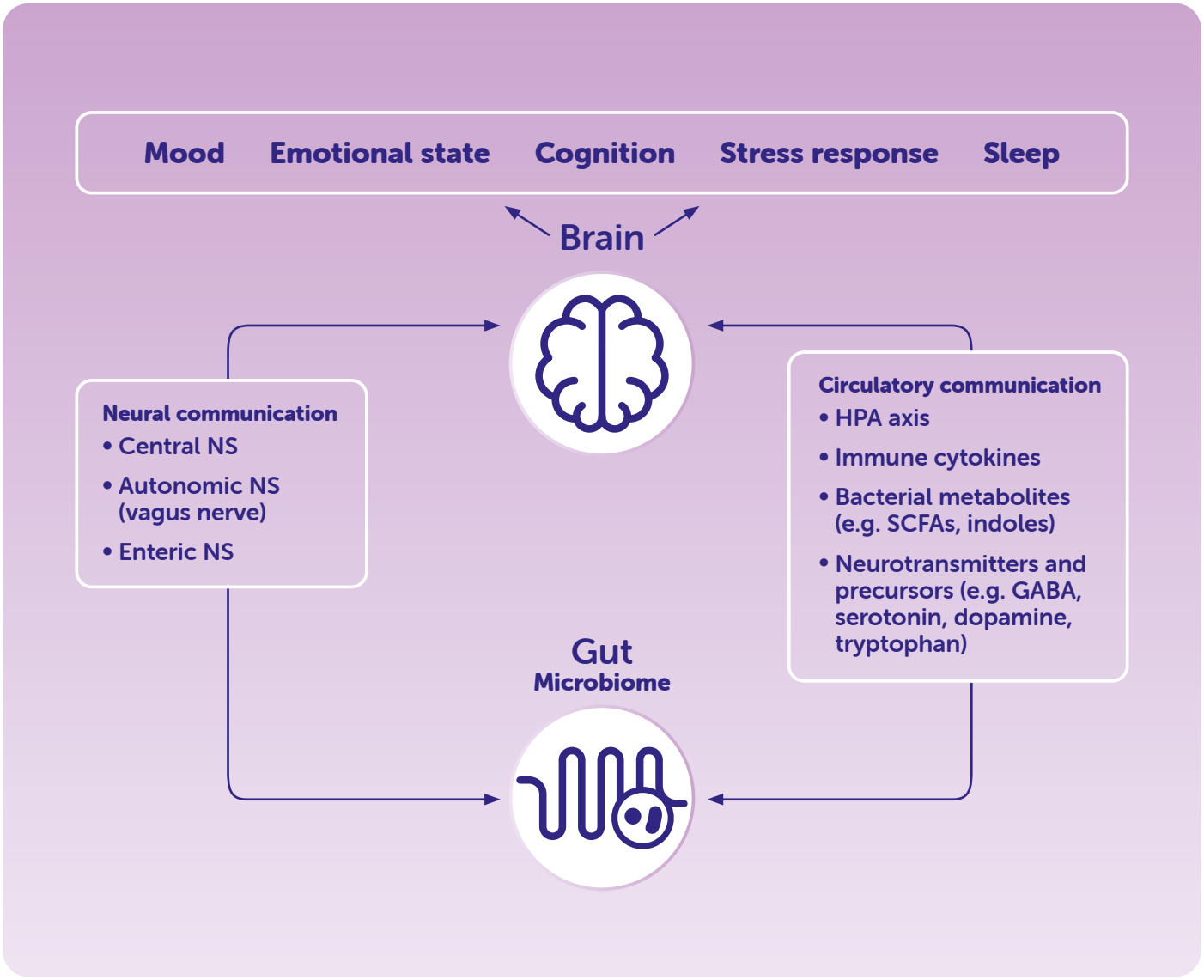
Protexin® VETERINARY | Smarter pet care, powered by biotics.

SereniCare® for Dogs & Cats

Calming support for dogs and cats, containing a novel postbiotic blend, Alpha-casozepine (Hydrolysed Milk Protein) and L-tryptophan. Formulated to help manage stress, anxiety and gut health.

PROTEXIN® BIOTICS
GOOD GUT HEALTH
✔PREBIOTICS
✔POSTBIOTICS

The gut-brain-microbiome axis



A bidirectional communication exists between the gastrointestinal (GI) tract (including the microbiome that resides within it) and the brain; this is called the gut-brain-microbiome axis (GBMA). It is comprised of multiple pathways meaning that the emotional and cognitive centres of the brain are inherently linked to the peripheral actions of the gut and the microbiome, and vice versa.[1]

Neural communication occurs via the central nervous system (CNS), enteric nervous system (ENS) (often referred to as the 'second brain') and autonomic nervous system (primarily via the vagus nerve),[1,2] whilst circulatory pathways include the hypothalamic-pituitary-adrenal (HPA) axis, immune system, and endocrine and bacterial factors.[1-3] These complexly intertwined pathways form the GBMA and allow the brain to influence

GI function, and the gut to impact behaviour, cognition and mood states.[1]

Within the GI tract, the gut microbiome (GM) largely influences the GBMA by producing neurotransmitters (and their precursors) such as γ-aminobutyric acid (GABA), serotonin and dopamine and metabolites such as short-chain fatty acids (SCFAs). Some of these substances can act locally on the ENS or signal to the CNS through vagal pathways, whilst others travel via the blood stream to impact brain function.[4]

As the gut's microbial composition can impact the synthesis and metabolism of neurotransmitters and their precursors, acting to support a healthy microbiome is important to promote normal brain function, mood and behaviour.[5]

Tryptophan and serotonin metabolism

Dietary tryptophan is an essential amino acid required for protein synthesis, whilst also being an important precursor for two major metabolic pathways to create kynurenine and serotonin.[6] Approximately 90% enters the kynurenine pathway, whilst the serotonin pathway competes for the remaining tryptophan, with only 1% being used for serotonin synthesis in the brain.[6,7]

Tryptophan metabolism and degradation, and thus serotonin synthesis, is strongly influenced by the composition of the gut microbiome.[5,9,10]

Tryptophan is the sole precursor of serotonin, therefore its systemic availability strongly determines central serotonin synthesis as serotonin itself cannot cross the blood-brain barrier (BBB).[5,8] As such, two distinct pools exist within the body: peripheral and central serotonin, with an estimated 90-95% produced with the GI tract.[5,6]

Peripheral serotonin acts locally in the GI tract to modulate intestinal motility and secretions, whilst also communicating with the CNS via neural and endocrine pathways to influence brain function.[1,3,10] Central serotonin is crucial for normal mood, social behaviour and cognition.[3,6,12]

The composition of the GM strongly influences tryptophan metabolism and degradation, and thus serotonin synthesis.[5,9,10] Certain bacterial species, such as some *Lactobacillus* and *Bifidobacterium* species, are able to convert tryptophan into serotonin in the gut; they can also suppress the kynurenine pathway, increasing tryptophan availability for central serotonin synthesis.[5,10] Furthermore, bacterial metabolites, such as SCFAs, promote endogenous serotonin production by intestinal enterochromaffin cells.[5,11,12] The GM is therefore crucial in regulating normal function of the GBMA.

The GABAergic system

Within the mammalian CNS, GABA is the predominant inhibitory neurotransmitter, being utilised by approximately one-third of all CNS neurons; it has long been regarded as crucial for the regulation of anxiety responses.[13,14] Hence, exogenous compounds that act to modulate the GABA receptor are known to promote calming effects.[13,15]

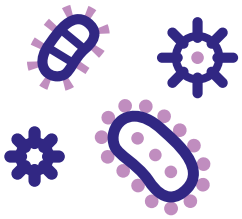
Postbiotics

With *'post'* meaning after and *'bios'* meaning life in Greek, the term *'postbiotics'* refers to inanimate or inactivated microorganisms and/or their components (cell walls, membranes, exopolysaccharides, cell-wall anchored proteins, pili, etc.) which have been shown to confer a health benefit to the host.[16]

The concept of postbiotics grew from the observation that many of the microbiota's effects could be delivered through the actions of their various components and not only the live bacteria themselves. Postbiotics appear to provide a novel and practical way to support both the microbiome and many other aspects of host health.

Postbiotics:

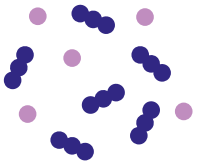
may contain intact non-viable microbial cells



and/or structural components of microbial cells

cell-wall anchored proteins, pili, cell walls, membranes etc.

with or without metabolites

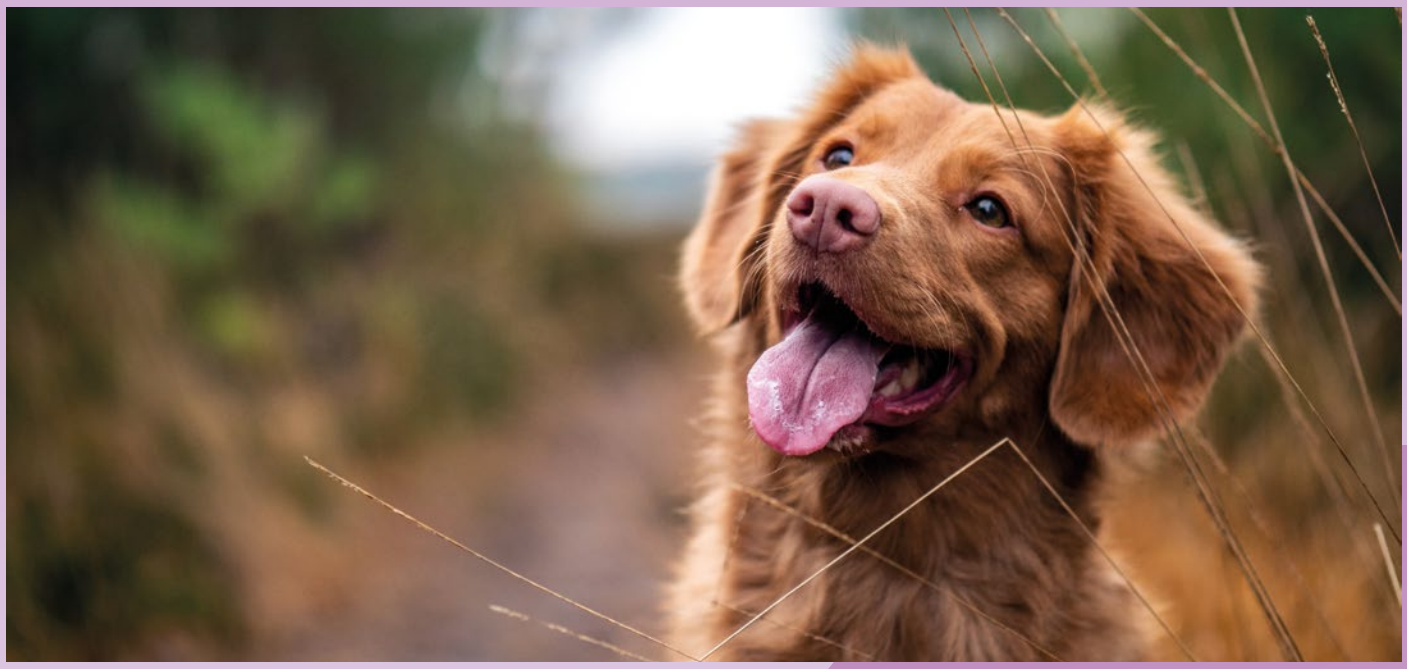


short-chain fatty acids, peptides, bacteriocins etc.

Introducing SereniCare

Postbiotic calming blend

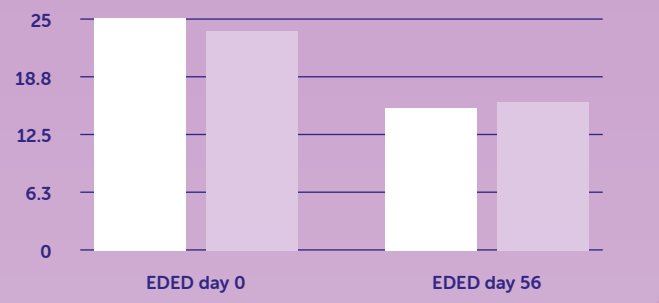
Given the importance of the gut microbiome in GBMA signalling, manipulation of microbial populations in the GI tract can help to support normal behaviour and discourage anxiety. Heat-treated postbiotics *Lactobacillus rhamnosus* CECT8361 and *Bifidobacterium longum* CECT7347 have been shown to help modulate anxiety to support normal behaviour patterns in zebrafish,[17] an animal model commonly used for studying anxiety-related phenotypes. The latter postbiotic strain has also demonstrated efficacy in supporting gut barrier function and offsetting oxidative stress in *C.elegans*.[18]



Alpha-casozepine (Hydrolysed Milk Protein)

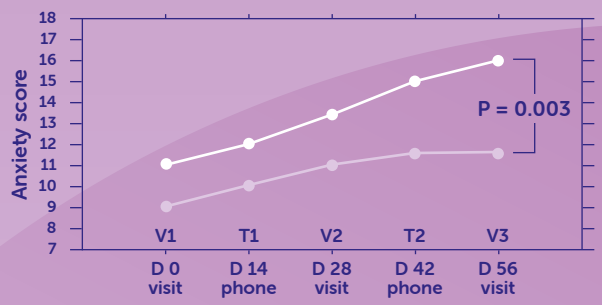
Alpha (α)-casozepine is a bioactive peptide derived from αs1-casein, a protein found in cow's milk; it was discovered whilst conducting research into the calming effect of milk in babies. Likely through interaction with the GABAergic system,[19,20] α-casozepine has shown a significant impact on managing stress and anxiety in numerous animal species, including humans, dogs and cats.[20-31] Many of these studies have demonstrated α-casozepine's efficacy through measurement of various physiological parameters and behavioural factors.[24-35]

Effects of alpha-casozepine versus selegiline on anxiety disorders in dogs



A graph to show the EDED score (a standardised anxiety metric) at score at day 0 and day 56 in anxious dogs taking α-casozepine or selegiline hydrochloride. NB a lower score represents less anxious behaviour. Graph constructed using data from Beata et al 2007.[22]

Effect of alpha-casozepine on anxiety disorders in cats



A graph to show anxiety scores of cats taking either α-casozepine or placebo. NB a higher score represents less anxious behaviour. Graph adapted from Beata et al 2007.[21]

V1, V2, V3: vet visits at day 0, 28 and 56. T1, T2: phone follow-ups at day 14 and 42

L-tryptophan

L-tryptophan is an essential amino acid and the sole precursor to both serotonin and melatonin. Systemic availability of tryptophan is essential for serotonin synthesis within the CNS, as serotonin itself cannot cross the BBB.[5] Tryptophan has been implicated as a key molecule for the regulation of normal mood, cognition, and sleep.[3,6] Studies have demonstrated tryptophan's ability to support normal behaviour in dogs and cats[36,37] and help regulate a normal stress response in various other species.[38-40]

Fibersol™

Fibersol is a resistant maltodextrin which bypasses enzymatic digestion in the small intestine to act as a prebiotic to the bacteria within the colon.[41] Fibersol's slower fermentation rate means that it has a prolonged period of SCFA production and therefore supports the microbiome for a longer duration. SCFAs are important metabolites for the maintenance of intestinal health and normal gut-brain communication.[1,2,42,43]

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SereniCare is suitable for use in situations such as:

- **Noise sensitivity** (fireworks and thunderstorms)
- **Stressful situations** (vet visits, moving home, kennels/cattery, travelling)
- **Separation anxiety**
- **Social fear** (unfamiliar visitors)
- **General anxiety**

Instructions for use

Begin supplementation with SereniCare 2 weeks prior to expected anxious event.* Give once daily according to body weight. Can be repeated 90-120 minutes prior to an expected anxious event. SereniCare is suitable for long-term use alongside appropriate behavioural training. Amount may be increased or decreased as directed by your vet.

*Individual animals can vary. Effects may be seen sooner in some animals, though may take up to 6 weeks in others.

Weight	Daily amount
<10kg	½ sachet
10-25kg	1 sachet
25-50kg	2 sachets
>50kg	3 sachets

87.5% recommend SereniCare to their family & friends
HomeTesterClub.com

After 6 weeks testing SereniCare:

67% agreed their pet's **nervousness significantly improved** after using SereniCare

70% agreed SereniCare successfully made their pet **more calm**

"This product has really helped calm my dog. Especially when I take her for a walk and other dogs or people approach her, she's not so scared and won't growl at them anymore. She is now so placid and I will continue to use this product, amazing stuff!!"

Jade – Home Tested

★★★★★ 10/10

For references please visit protexinvet.com/serenicare-refs or scan

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