

# **Behavior Therapies: From Natural Supplements to Pharmaceuticals**

Melissa Spooner, LVT, VTS (Behavior), BS, KPA-CTP

Leader Dogs for the Blind

Bloomfield Hills, MI

An anxiolytic is defined as any drug or supplement used to treat chronic or acute anxiety. Medications or natural supplements used as anxiolytics can be helpful adjuncts for behavior modification if the animal's fearful or anxious behavior is so intense that it interferes with learning or other normal activities. Though both nutraceuticals and pharmaceuticals play important roles in animal behavior, it is important to understand the different options and how they can most effectively be implemented into a behavior modification plan. The information offered in this presentation should act as a guide, outline or overview of possible applications in a clinical setting.

Over the last five years there has been an increased desire to treat medical issues using natural remedies and alternative medicine. This desire has slowly moved from the human to veterinary world. It is the goal for many pet owners to improve their pet's medical or behavioral status without altering their pet's personality negatively. It is also hoped that natural supplements are a healthier choice and will cause less harm to the body. Nutraceutical Medicine is defined as the use of micronutrients, macronutrients, and other nutritional supplements as therapeutic agents. Communication on the potential risks and benefits from the use of these compounds within the context of a valid veterinarian/client/patient relationship is important. Continued research and education on the use of nutraceuticals in veterinary medicine is advised.

Adaptil® by Ceva formerly known as DAP is a synthetic version of a pheromone that is excreted from bitches that are nursing their offspring. Adaptil assists new born puppies to search for, orient and bond to their mother. The pheromone elicits a soothing and calming response to the puppies, however it is thought that the pheromone in the synthetic form can be beneficial for dogs at any age. Adaptil is available as a veterinary Over the Counter (OTC) product. As of today, Adaptil can be found in three different forms; a spray, plug in diffuser and disposable collar. Each works slightly differently. The rate of onset and the longevity varies with each product. Because the rate of onset is generally fairly short (15-30 minutes) depending on the product it can be classified as a situational anxiolytic that can be used on an as needed basis. While the Adaptil collar and diffuser last for four consecutive weeks, the spray can be used as needed in a specific location and should last for several hours before needing to be re-applied.

Rescue Remedy is another natural supplement that has both oral and topical applications. It is often selected as a first form of treatment by many pet owners because of its availability and longevity. The ingredients of Rescue Remedy include Impatiens, Star of Bethlehem, Cherry Plum, Rock Rose and Clematis. This is an alcohol based product and the company suggests that some pets may be sensitive to alcohol, in which case, Rescue Remedy should be diluted before it is administered, or the alcohol-free Rescue Remedy should be selected as an alternative. Similar to many of the other behavior targeted nutritional supplements, Rescue Remedy can be used for pets that experience anxiety during visits to the vet, separation anxiety, noise phobias such as thunderstorms and fireworks, excessive barking, hissing or being kenneled. Shock, trauma, obsessive cleanliness, mistreatment, constant licking, and self-mutilations are listed as ailments that can be treated by Rescue Remedy. The solution can be given to pets orally, in their food or water bowl. Rescue Remedy can also be rubbed directly on an animal's nose, ear or paw. It can be used for an immediate calming effect in any stressful situation.

Harmonease contains natural extracts of *Magnolia officinalis* and *Phellodendron amurense* combined in a chewable tablet. Harmonease helps dogs to overcome stressors such as noises and fear causing situations. The intent of Harmonease is to decrease anxiety without causing lethargy, which is a desirable state for maximum learning. Harmonease has been evaluated in kenneled dogs and shown to stop stereotypical behaviors, such as lick granulomas, spinning and cowering within five days of administration. Dosing directions are recommended once daily as follows; for dogs up to 50 lbs, give ½ tablet and for dogs over 50 lbs give 1 tablet. For noise phobia, administration is recommended 7 days before the anticipated event and throughout the necessary period of time. As with any anxiolytic, Harmonease should be used under the guidance of a veterinarian and in conjunction with a behavior modification plan.

Anxitane is a product from Virbac which sole ingredient is Suntheanine brand L-Theanine in a neurologically active chewable form. Anxitane promotes relaxation in pets exhibiting nervousness, anxiety or response to environmentally induced stress. This nutraceutical targets undesirable behaviors such as fear on walks, people and other animals. It also improves anxiety or stress associated with change in family situation or environment, episodic fear such as; noise phobias grooming, car travel and veterinary visits. The goal of this supplement is to significantly reduce stress related reactions; however Virbac recommends that this product should not be used for patients with severe phobias, separation anxiety or aggression. One reason that this product may be selected over some of the other options is due to its highly palatable form, a poultry flavored tablet, which makes administration to both dogs and cats very easy. There are also no known interactions with other therapeutics. It is recommended that Anxitane is used for no less than 60 days to fully assess the effectiveness and so that maximum results can be observed. Anxitane is available in two different sizes; small (50mg) for dogs and cats under 22lbs which is administered ½ tablet every 12 hours, and medium/large (100mg) for dogs

22.1-55lbs, the dose is ½ every 12 hours and dogs that exceed 55.1 lbs should be given 1 full tablet every 12 hours. The tablets are scored and can be easily divided to achieve the desired dose.

Composure is a nutritional supplement by Vetri-Science, which combines three natural ingredients. Similar to Anxitane, Composure contains Suntheanine brand L-Theanine, which is a naturally occurring amino acid found in green tea and it has been researched extensively for its ability to reduce stress, anxiety and unwanted behavior. It helps the body to produce other calming amino acids such as Dopamine, GABA and Tryptophan and helps bring certain neurotransmitters into better balance. Studies done on L-Theanine showed that dogs reduced anxiety-related behavior without adverse effects or drowsiness; dogs were alert, playful and calmer than expected given their situations, which are the desirable effects when utilizing an anxiolytic. L-Theanine also promotes calming and relaxation and reduces irritability and low mood states. The second ingredient is Colostrum Calming Complex, which is an isolated form of colostrum proteins, which have a calming effect on animals. These bioactive proteins have been found to support cognitive function and support stress reduction. The Colostrum Calming Complex works synergistically with the L-Theanine in this formula to promote relaxation and cognition in dogs. Lastly, Thiamine helps manage stress and reduces irritability. Thiamine (Vitamin B1) has been shown to affect the central nervous system to help calm and soothe anxious animals. A lack of Thiamine can cause mental confusion, muscular weakness, muscle spasms, nervousness, and weight and appetite loss during periods of stress. The Composure formula is available in two forms; a suspension and palatable bite sized chews. Recommended directions for the suspension in cats is ¼ teaspoon twice daily. Dogs under 25 lbs ¼ teaspoon twice daily, 26 - 49 lbs ½ teaspoon twice daily, 50 - 75 lbs ¾ teaspoon twice daily and 76 lbs and over 1 teaspoon twice daily. Recommended directions for the chews are for pets up to 25 lbs 1 chew daily, 26-50 lbs 1 chew daily, 51-100 lbs 2 chews daily, over 100 lbs 3 chews daily. Both forms of Composure can be used either as needed for immediate support or on a daily basis for on-going support. During times of increased stress it is safe to double or triple the directed amount.

Novifit also by Virbac, is targeted towards a slightly different area of behavior. Its active ingredients are S-Adenosyl-L-Methionine-Tosylate Disulfate also known as SAME. Novifit is designed to support cognitive function of aging dogs and cats. These tablets help to control behavioral disorders related to brain aging such as disorientation, changes in social interactions with people and other pets, changes in sleep-wake cycles and loss of housetraining skills. They are a highly pure and stable form of SAME (NoviSAME) presented in an enteric-coated tablet. As a nutraceutical, it is a first line treatment of behavioral problems associated with cognitive decline for both dogs and cats. Novifit is available in three different sizes; small (100mg) for dogs and cats under 22lbs, medium (200mg) for dogs 22.1-44lbs, and large (400mg) for dogs 44.1-88lbs. The tablets can be given once a day in food, but should not be crushed or divided up into smaller pieces.

Not all behavior problems will demonstrate the desired level of improvement by using a natural supplement as therapy. Instead they may require a prescribed short term or long-term pharmaceutical anxiolytic. Some problems such mild noise phobias (thunderstorm & fireworks), activity or location specific (veterinary hospitals or grooming visits) anxieties may need only to be treated on an as needed basis. Using a short-term medication may efficiently treat this diagnosis. Under the supervised care of a veterinarian, a patient's anxiety status can be thoroughly assessed and the appropriate method of treatment can be determined.

Alprazolam and Diazepam are in the same drug category called Benzodiazepines. Benzodiazepines are anxiolytic medications with rapid onset of action that last for a few to several hours depending on the specific drug and the species. They are frequently used as augmenting agents for SSRIs or SNRIs in the treatment of anxiety disorders but also can be prescribed as a standalone drug. Benzodiazepines are metabolized by the liver and excreted into the urine. They should be used for situational anxiety because of the short duration of onset. Although Alprazolam and Diazepam are in the same family, there are significant differences between the drugs so they may be selected for different reasons. Alprazolam, which is the generic for Xanax is available in both tablet and suspension form. It is often prescribed to improve symptoms related to noise phobia, separation anxiety or generalized anxiety. Alprazolam is most likely to be effective when given 30-60 minutes before the occurrence of the earliest stimuli that elicits a fear response, and may remain in the system for 2-4 hours. Dosing recommendations are 0.02-0.1mg/kg every 6-8 hours for dogs and 0.02-0.05mg/kg for cats as needed for anxiety. If a patient has been receiving Alprazolam daily for several weeks, discontinuation should be gradual, and conducted over a period of at least one month. Diazepam (Valium) has been used in many areas of veterinary medicine. Diazepam has a CNS depressant effect that results in calming, sedative, skeletal muscle relaxation and anticonvulsant effects. Although Diazepam is available in multiple forms, oral administration is the preferred route for improvement of behavior problems. The drug reaches full levels at 30-120 minutes after administration and may last 2-3 hours. Dosing recommendations are 0.5-2mg/ kg every 6 hours for dogs and 0.2-0.5mg/kg every 8-12 hours for cats as needed for anxiety. Previously Diazepam was the drug of choice used to treat cats for spraying, anxiety motivated inappropriate elimination, general anxieties and fear related aggression, however after it was determined that it was more likely to cause hepatopathy, it's use was decreased. Similar to Alprazolam, patients receiving long-term daily treatment with Diazepam should be gradually weaned before completely discontinued. All of the drugs in the benzodiazepine category are controlled substances with the potential for human abuse. When drugs in this category are prescribed they should be monitored closely. If medications in this class are going to be prescribed over a long period of time only a limited amount of medication should be dispensed as needed, and when additional refills are requested, the previous

amount dispensed, previous date issued and the doctor's directions should be compared closely. Benzodiazepines are generally safe drugs to use with minimal side effects. The side effects reported most often are lethargy, hyperactivity and ataxia. Benzodiazepines have the possibility to cause disinhibition, or fearful animals could become more aggressive. For this reason it is important to monitor the patient closely while this medication is in use, and appropriate behavior modification should be implemented along with any behavior medication. Fulminant hepatic failure associated with oral administration of Diazepam was reported in some feline patients so blood work should be done on cats to check liver values. Hyperphagia may also be reported in both dogs and cats but in some cases that is a side effect that may be considered desirable at times.

Acepromazine falls under the antipsychotic drug category. It is a tranquilizer that causes decreased motor function and reduced awareness of external stimuli. Patients that are prescribed Acepromazine will appear sedated and possibly lethargic, which can be beneficial in some areas of behavior treatment. Classical antipsychotics can calm anxious patients and may be considered for pets that are destructive to themselves or their surroundings. Acepromazine also has an antiemetic effect so it may be recommended for dogs that experience car ride anxiety characterized by nausea or vomiting. However, there is some concern whether or not Acepromazine makes an appropriate behavior modification drug. Since it causes sedation, it may limit the animal's ability to learn and repeat desired behaviors in difficult situations. Ataxia, hypotension, decreased seizure threshold, and bradycardia are all possible side effects that may occur after administration of this drug. Any patient that is prescribed Acepromazine should be monitored closely. Recommended doses for Acepromazine is 0.5-2mg/kg orally every 8 hours or as needed for dogs and 1-2mg/kg orally as need in cats.

Situational anti-anxiety supplements or medications may not always be suitable in every case. Patients that experience ongoing anxiety, extreme phobias or when quality of life is severely impacted by their behavior may require long term drug therapy. There are several drug classes to choose from when selecting the appropriate drug for the patient.

SSRIs selectively block the reuptake of serotonin back into the presynaptic neuron. Consequently they increase the levels of serotonin in the synapse. Fluoxetine has been used most commonly in the treatment of behavior problems in companion animals, particularly those with anxiety disorders, such as separation anxiety and aggression, however it may be utilized to decrease reactivity, vigilance and compulsive disorders. Fluoxetine is a Selective Serotonin Reuptake Inhibitor (SSRI) generic for Prozac or Reconcile, a veterinary brand name. Drugs such as Fluoxetine found in the SSRI category are intended as long term anxiolytics, because they may be used over several months, years or lifelong. When Fluoxetine is prescribed it should be explained as a commitment to the client. Improvement from this medication may take 4-6 weeks from the start date to assess, and it is important for clients to have appropriate expectations of the drug. Using a veterinary brand name drug such as Reconcile can have several advantages over choosing the generic version. One important advantage is the palatability of the tablet, which is made from beef flavoring and can ease administration to an already anxious animal. The second advantage is the extensive research that has been completed to fully understand the effects, expectations and benefits of the medication. The company also offers veterinary education and support to prescribers. Despite the many positive aspects of using Fluoxetine it does have several side effects that both prescribers and veterinary staff should be aware of. Lethargy and decreased appetite are most often observed though they are generally transient and reported during the first 1-4 weeks of treatment. Vomiting, diarrhea, changes in urinary frequency, insomnia and sedation are also possible side effects. Dosing the medication every other day for the first 7-10 days can lessen side effects. Food may delay its absorption by 1-2 hours, so it may be most effective if given on an empty stomach. The combination of Fluoxetine and MAOIs can result in serious and sometimes fatal drug interactions. These two medications should never be given together. However, combining an SSRI with a benzodiazepine may enhance the drugs to achieve a better effect. Recommended dosing of Fluoxetine is 0.5-2mg/kg once daily. Paroxetine is another SSRI used to treat anxieties involving social interactions; it is very similar to Fluoxetine. Dosing recommendations are 0.5-1mg/kg orally 1-2 times daily. Side effects include sedation, increased anxiety, animals seeming withdrawn, loss of appetite and the possible lowering of seizure threshold. Urine retention and constipation are also possible side effects. It may have the advantage of being more calming and therefore more preferable for some anxiety disorders. It is less likely to lead to agitation and insomnia compared to Fluoxetine. Paroxetine has a much shorter half-life than Fluoxetine. After the desired level of behavioral improvement is achieved the patient should slowly be weaned off of the SSRI, over a 4-6 week period. If medical side effects are observed that suggest interference from the medication, it can be safely stopped abruptly.

Another major class of drugs used for long-term behavior therapy is Tricyclic Anti Depressants, which block the reuptake of norepinephrine, dopamine, and serotonin into the presynaptic terminal. They effectively increase the level of neurotransmitter in the synapse. They are commonly used in dogs to manage behavior problems ranging from aggression to urine marking, repetitive behaviors, and separation anxiety. In cats, TCA's can be used to treat certain forms of aggression, urine spraying, excessive vocalization and grooming. Clomipramine and Amitriptyline are well known drugs in this category. Clomipramine, also known as Clomicalm, is one of two drugs licensed in the United States used to improve separation anxiety, (the other is Reconcile). Clomipramine is unique from other TCA's because it is the most selective inhibitor of serotonin reuptake. There is wide dose range offered for Clomipramine. Recommended doses for cats is 0.125-1mg/kg and dogs 0.5-2mg/kg divided every 12 hours depending on the diagnosis. Amitriptyline, (Elavil), may be used for diagnosed separation anxiety and generalized anxiety in both dogs and cats. Because of its sedative, anti-anxiety, anti-histaminic effects as well as its potential improvement for chronic pain it may be useful in

some self-traumatic disorders such as early stages of ALD-type lesions in dogs. Typical dosing for Amitriptyline is 50-150mg per day which is likely divided into 12 hour doses. For both Clomipramine and Amitriptyline, behavioral improvement will take 2-4 weeks to assess and if the desired improvements are not observed by 6-8 weeks, the dose may need to be increased. Potential side effects include cardiac arrhythmias and seizures. Urinary retention and dry mouth may also occur during therapy. Amitriptyline is also notoriously known for being very bitter tasting, it can be difficult to mask in food and both dogs and cats may become disagreeable to taking it. Both Clomipramine and Amitriptyline should be slowly weaned before they are discontinued so that the undesired behavior problems do not reoccur.

Most psychoactive medications are used off-label for animals. Only a few medications, such as Fluoxetine (Reconcile, Lilly) and Clomipramine (Clomicalm, Novartis Animal Health), are indicated for specific use in dogs.

Another class of drugs that is important to be aware of is Azapirones. Azapirones are described as anxiolytic instead of anxiolytics because they do not cause sedation, which may occur during treatment with other classes. Similar to some of the TCAs and SSRIs, Buspirone can be used to treat generalized anxiety, inappropriate elimination, (specifically feline urine spraying), separation anxiety and some forms of aggression. A veterinarian may choose to treat with Buspirone when the patient's anxiety is decreased as it can often make them friendlier and more likely to seek attention. The prescriber should be aware that inhibition could lead to aggression. However, the desired effects may not be achieved by using Buspirone alone. Often Buspirone may be combined with SSRIs or TCAs in order to have an optimal effect. Azapirones should not be combined with Monoamine Oxidase Inhibitors, (MAOI's), because of the potential for toxicity. Dosing for Buspirone for dogs is 0.5-2mg/kg every 8-24 hours. The feline dose varies slightly. It can be prescribed as 2.5-7.5mg/ cat every 12 hours or 0.5-1mg/kg every 12 hours. The rate of onset is shorter than other long-term behavior therapy drugs and behavioral improvement can typically be observed in 1-4 weeks.

Prior to starting any new behavior medications it is always recommended that baseline blood work be performed. It is important to understand how the drug that is being prescribed is metabolized and excreted and select appropriate blood work accordingly. An extensive chemistry panel and complete blood count are usually recommended. Depending on the prescribing physician, signalment and history of the patient, additional blood work may be indicated. Age, history and current health status of the patient may also determine how often blood work is repeated. Schedule guidelines for blood work can be as follows: 1-3 years old, once yearly, 4-9 years old, every 6 months, and 10 years and above every 3 months. The prescribing physician should ideally perform a physical exam at regular scheduled intervals. Depending on the reason for the patient being on behavior medications, an observational physical exam may be the only reasonable option. An observational physical exam will allow the physician to assess the patient from a comfortable distance. Gait, body condition score, skin, coat and neurologic status can all be assessed in this manner, however it should be the long term goal of the veterinary staff and client that patient be desensitized for physical exam at future medical visits. Grouping multiple medical procedures together for patients that are fractious during veterinary visits, such as blood draws, vaccinations, nail trims and physical exams, may prove to be easier for the patient to cope with. This will assist in decreasing the amount of "negative" veterinary interactions, although some patients may do better if the procedures are scheduled on separate visits.

Veterinary technicians can play a very important role assuring that multiple medications or other treatments are not prescribed where contraindicated. Patients that are being treated by various doctors run the risk of two or more medications being recommended simultaneously when they should not be paired together. It will be the job of the veterinary technician to work closely with clients on obtaining a complete behavior and medical history and reporting your findings to the veterinarian. The owner should be encouraged to list all medications that the patient may be taking. This list should include the medication strength, frequency, when it was started, last dose given or any medications that have been discontinued recently. Any nutraceutical or over the counter medications that are being administered should be included in this list. This drug list should be updated anytime medications are added or altered and anytime the patient is seen at the hospital. If possible, an alert should be made in the patient's chart in both digital and hard copies. Fluorescent stickers are an inexpensive yet effective method of alerting all veterinary staff that the patient is taking a medication that may be contraindicated with other medications. As with children, all medications should be stored in tamper proof containers that are out of reach. Due to several behavior medications now being made highly palatable for the patient, they should be kept where family pets do not have access to them.

Concerns arise when SSRIs, MAOs or TCAs are combined with other medications or supplements that may cause excess serotonergic activity at the central nervous system (CNS) and peripheral serotonin receptors. This is a potentially life-threatening adverse drug reaction that known as Serotonin Syndrome, may occur following therapeutic drug use, inadvertent interactions between drugs, or overdose of particular drugs. The most serious cases result when an SSRI are combined with an MAO inhibitor, which decreases serotonin metabolism, and a serotonin receptor agonist, such as Buspirone, a TCA which is a non-selective serotonin reuptake inhibitor, or Meperidine, Tryptophan or Dextromethorphan. There is still much to be learned about how Serotonin Syndrome affects animals, we do know that it has the potential to be fatal and precautions should be taken to avoid this possibility.