

## St. John's Wort (*Hypericum Perforatum*) as a Psychoactive Herbal Medicine for the Treatment of Behavioral Disorders in Dogs

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### Commentary

St. John's wort (*Hypericum perforatum*) is an herbaceous and perennial plant that is native to Europe, West Asia and North Africa, which have been widely used as an herbal medicine [1]. It is one of the most largely used medicinal plants around the world [2], being one of the best characterized herbal medicines [3]. St. John's wort is the only herbal alternative to synthetic medicines for the treatment of depression [4]. In Europe, it is widely used to treat psychiatric disorders, including anxiety and depression [5]. In Germany, sales of this herb exceeded those of all antidepressants combined [6].

St. John's wort is an accepted alternative to synthetic antidepressants or even behavioral therapy for the treatment of depression [7,8]. Significant clinical results were demonstrated in a study that conducted a meta-analysis based on 23 clinical trials, with 1757 outpatients suffering from mild or moderate depression [9]. The effects of St. John's wort in this study were better than placebo and just as effective as standard antidepressants [9]. In addition, similar anxiolytic effects of St. John's wort have also been demonstrated [10,11]. Thus, this herb is the most recognized and used herbal medicine in the treatment of depression and anxiety in humans, with well-studied active principles, effects, mechanisms and drug interactions [12,13].

Furthermore, St. John's wort is not associated with serious adverse reactions in humans and appears to be well tolerated in our body. This herb triggers fewer adverse reactions than synthetic drugs for the treatment of psychic disorders. Adverse reactions commonly include gastrointestinal symptoms (0.6%), allergic reactions (0.5%), fatigue (0.4%) and restlessness (0.3%), with phototoxicity reported in cattle and sheep that fed on this herb. In addition, St. John's wort also has a number of other effects that can also be beneficial. It can be used to treat stress, sleep problems, nocturnal enuresis, bacterial and viral infections, respiratory conditions, peptic ulceration, inflammatory arthritis, cancer and skin wounds, besides other positive effects more recently reported. Even a significant analgesic effect has already been demonstrated for St. John's wort.

Although the action mechanism of St. John's wort has not yet been fully elucidated, some studies have shown that such mechanism is linked to the inhibition of serotonin reuptake, in addition to the effect as norepinephrine inhibitor and in the dopamine reuptake. In veterinary medicine, serotonin and norepinephrine uptake inhibitors have been shown to be effective in treating problems related to separation anxiety in dogs, which reveals the potential of using St. John's wort, with a similar mechanism, for the treatment of this disorder in dogs. Moreover, even though there are still few studies of this herb as a psychoactive agent for dogs, studies in rats have shown great potential for the treatment of both depression and anxiety.

Another aspect that should be highlighted is that, even with few studies in dogs, this herb has been recommended and used in practice by veterinarians. There are even specialized sites which are at least relatively reliable that show the advantages of using this herb in the treatment of behavioral disorders in dogs. This, in addition to

the fact that St. John's wort has been traditionally used for so long in folk medicine, especially considering oriental medicine, reinforces its potential as an herbal medicine for dogs.

However, as St. John's wort has been reported as an herbal medicine that potentially can involve in several drug interactions, also in dogs, it is important evaluating each individual case and particular context and taking this into account when recommending the use of this herb for the treatment of behavioral disorders in these animals. In fact, *H. perforatum* interacts with some important drugs, such as cyclosporine, HIV protease inhibitors, cytostatic substances, anticoagulants, contraceptives and oral hypoglycemic agents. Despite this, it is worth noting that not all drug interactions are, in fact, relevant for dogs. For example, the drug interaction reported in studies with contraceptives is clearly insignificant in the case of dogs.

Thus, the potential of this herb to treat depression and anxiety in dogs is clear, and this is an area of investigation that still needs to be more explored to better determine the most appropriate dosages and potential risks specifically for dogs. This is not so simple, as the funding for such research probably will need to come from outside the pharmaceutical industry, because treatments based on herbal medicines cannot be patented, that is, financial incentives for scientific research that drives the pharmaceutical market are limited in this area. However, this should not preclude the development of new scientific research considering the use of St. John's wort as a psychoactive agent for dogs, as it has great potential for the treatments of behavioral disorders in these animals, including for canine cognitive dysfunction syndrome (CCDS), which is similar to Alzheimer's disease in humans.

We conclude that St. John's wort is a herbal medicine with great potential for the treatment of behavioral disorders such as anxiety and depression in dogs. Although there are still just a few studies with these animals, it is a phytotherapeutic that has been recommended by veterinarians and specialized websites to treat such disorders and that is widely recognized and used in the treatment of symptoms of depression and anxiety in humans. In addition, its potential as a psychoactive agent for dogs is emphasized by the advantages of promoting other potentially positive effects, besides causing fewer adverse reactions than synthetic drugs. However, more studies are needed to better determine specific concentrations, dosages and risks for dogs, which should probably depend considerably on funding from outside the pharmaceutical industry.

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