International Journal of Health Sciences and Research
Vol.12; Issue: 11; November 2022
Website: www.ijhsr.org
Review Article *ISSN: 2249-9571*

Plant Based Immunomodulators for Managing Stress in Animals - A Review

Preeti Srivastava[1], Farah Naz Faridi[2], Mudit Sharma[3]

[1]Assistant Professor, S.S. Jain Subodh P.G. College, Jaipur
[2]Independent Researcher
[3]Director, Mudrakshi Histology Centre, Jaipur

Corresponding author: Farah Naz Faridi

DOI: https://doi.org/10.52403/ijhsr.20221122

ABSTRACT

In animals the stress response is useful as a protection mechanism. The cause of stressful conditions in animals can broadly be due to physiological/ pathological conditions, infectious and metabolic diseases, predators, transportation, temperature, diet and chemicals. The oxidative stress is also generated in a number of clinical conditions in animals. The response to these stressors by the animal produces adverse effects on immune system, growth, production and feed conversion efficiency and a pivotal loss to livestock overall. The herbal immunomodulators help the animal to cope better during stress and related disorders by combating or restoring immune functions and play a vital role in animal's health by up-regulating the immune system. They effectively reduce the incidence and severity of disease episodes in populations of livestock that are immunologically impaired. The study of herbal immunomodulators is an emerging field in veterinary medicine where the herbs can be supplemented along with the therapy in order to minimize the losses due to clinical conditions in livestock and are helpful in preventing the body weight loss and in producing nutritious meat, eggs and milk. *Withania somnifera, Ocimum sanctum, Tinospora cordifolia, Asparagus racemosus, Emblica officinalis* among many others are known to possess immunomodulatory and anti-stressor properties. It increases physiological endurance and are beneficial particularly in stress-related disorders in animals. *Tinospora cordifolia* is known to have shown effect on diabetes in rats. *Asparagus racemosus* has shown antioxidant properties against damage induced by gamma radiation and development of intraperitoneal adhesions and macrophage modulation in animal models. Not only they strengthen the defense mechanisms against free radical damage during stress conditions they also induce immunostimulation. The *Ocimum sanctum* seed oil has been found to contain significant antioxidant and chemopreventive properties against 20-Methylcholanthrene induced fibrosarcoma in mice. Also, the herbal immunomodulators are found safe in acute and sub-acute toxicity studies. Therefore, the present article details the importance of herbal immunomodulators with their active ingredients and clinical indications in alleviating the stressful condition in animals and their role in better management of diseases in a futuristic approach.

Keywords: stress, herbal, immunomodulators, *Withania, Ocimum, Emblica, Tinospora*

INTRODUCTION

What are Immunomodulators?

Immunomodulators are drugs or compounds either biological or synthetic (recombinant DNA, vaccines and herbs) which modulate (change) the immune system of an animal. They can induce, suppress, amplify or inhibit any phase or part of immune system. Broadly they can be the suppressors (immunosuppressants) or can be the alleviators/enhancer (immunostimulators or immunoenhancers) of the immune system of an organism. A number of plant-based compounds like saponins, alkaloids,

glycosides and flavonoids are active ingredients of the herbal immunomodulator

Causes of stress in animals

1. Physiological or pathological process may lead to trauma, injury and septic shock.
2. Pyschophysiological stress when animal senses that a particular threat exists
3. Infectious disease conditions in animals due to virus, parasites or bacteria.
4. Production (metabolic) disease occurring during calving period
5. Transportation shock due to mishandling or overcrowding of animals.
6. Mixing with unfamiliar animals in new environment and lack of proper sanitation.
7. By extreme environmental or climatic conditions like heat or cold.
8. Mineral and nutritional deficiencies.
9. Mastitis, periparturient disorders and reproductive disorders.
10. Stress due to pregnancy and lactation.
11. Physical exercise or exercise- induced myopathies and hemolysis in race horses or in sledge dogs
12. 12.Exposure to xenobiotics, pesticides and hepatotoxic drugs like acetaminophen, carbon tetrachloride, etc
13. Stress and environmental pollutants including heavy metal toxicity such as lead, cadmium and mercury.
14. Predators as dogs, coyotes, and insects are stressful to animals and to their reproductive capacity.
15. Invasive collection of samples from animals- blood, rumen fluid etc.

Defense mechanism for combating stress

The immune system, endocrine system and Central nervous system of an animal interact and collectively respond to a stress stimuli in a coordinated manner. Many immunomodulators have effect on cytokine secretion and expression which in turn either suppress or enhance the immune system. The most commonly modulated cytokines are Interleukin- 1, Interleukin-6, Tumor Necrosis Factor and Interferon. Number of herbal immunomodulators are studied and their role as anti-stressor, anti-oxidant and adaptogen has been reported in animals. They are also useful in controlling parasitic infection in livestock and poultry. A few most common and important herbal immunomodulators as anti-stressor in animals are reported here.

Withania somnifera- This wonder plant also known as Indian Ginseng has been used since ages in almost every immune disorder in animals and also as a remedy for several ailments. Ashwagandha (Sanskrit) is a well known anti- stressor besides being anti-fatigue, anxiolytic. *Withania somnifera* has been found to influence the TNF expression. The adaptogenic potential of *Ocimum sanctum* and *Tinospora cordifolia* as a phytotherapy has been postulated as a new therapeutic approach by combining scientific, modern and traditional medicines for combating the H1NI/Swine influenza A. The immunomodulatory effect of *Withania* was seen in mice for immune inflammatory systems. [(1)] The potent anti stressor activity of *Withania somnifera* has been studied in rats. [(2)] Various withanolides have been isolated. Withaferin A and 3- b -hydroxy-2, 3-dihydrowithanolide F has anti stressor and anti tumor activity besides being anti-bacterial. The antioxidant effect of glycowithanolides was reported for the tardive dyskinesia, for chronic foot shock stress induced changes in rat brain. [(3)] The anti-inflammatory activity of this plant has been reported [(4)] and also its immunostimulatory activity. [(5)] The antibacterial property of WS has been reported against *S. typhimurium* and *E. coli*. [(6)]

Ocimum sanctum- The leaf extracts of OS have antipyretic, anxiolytic, analgesic and antiarthritic activities. The antistressor property of *Ocimum* has been elucidated by many workers. Similarly, OS leaf extracts was found to reduce swimming stress induced ulcers in albino rats and was found to have antioxidant and antiulceric activity and ulcer healing properties in animal models. [(7,8,9)] The fixed oil of OS was found

to have anti-inflammatory as well as anti-ulceric properties in the animal models of albino rats and guinea pigs due to its anticholinergic and antisecretory effects. [10] The protective nature of OS can be attributed to its property of suppression of free radicals. The in vivo and in vitro studies regarding the ability of OS to scavenge free radicals and anti-lipid peroxidase activity and antioxidant activity have been reported. [11] OS can prove to be a drug of choice without any noticeable toxicity effect on organism as most of the anti-inflammatory drugs in the market are ulcerogenic.

The major component euginol (essential oil of OS) was found to have antifungal, anti aflatoxigenic properties [12] and was found to be safe to be used in mammalian models and also as a safe plant based alternative to synthetic preservative in the market.

The chemopreventive activity of seed oil of OS against 20-methylcholanthrene induced fibrosarcoma tumors in mice and the detoxifying effects on reactive carcinogenic species in mice has also been reported.[13] Similarly the hydroalcoholic extract of OS was found effective against CRS (Chronic Restraint Stress) induced rise in plasma cAMP level, myocardial Super oxide Dismutase and catalase activity in rats. [14] The OS has found to be effective against the psychological and oxidative stress leading to cardiovascular risk and diseases. [15,16]

In another study the alcoholic extract of OS was found to be active against the noise stress by bringing back to normal the alleviated level of neutrophils and plasma corticosterone due to noise stress. [17,18]

Similarly the ethanolic extracts of OS reduced the noise induced changes in the two central cholinergic system in the four areas of brain of albino rats suggesting its protective nature against the noise stress [19] and similar reduction was found in the stress indices like plasma corticosterone, in organ weight of rats by acute noise stress and reduction in leukocytes.[20,21,22] The suppression or scavenging effects of free radicals by the OS gives this herbal immunomodulator its protective property.

Emblica officinalis- The mixture of *Ocimum sanctum* and *Emblica officinalis* was found to be an effective immunomodulator in gaining weight in immunosuppressed broiler birds. [23] The medicinal plant is good for anti-hepatitis, anti-oxidant, anti-stressor, anti-cancer, anti-tumor and regulation of stomach function. The plant is also regarded as a traditional immunomodulator and a natural adaptogen.

Many herbal immunomodulatory preparations are widely available in the market which are free of side effects and are safe to use in animals like poultry, turkey, rabbits, pigs and other livestock and have anti-stress, anti-oxidant and adaptogenic properties. Immuplus has *Withania somnifera*, *Tinospora cordifolia*, *Ocimum sanctum* and *Emblica officinalis* as its constituents and has been found to increase paraspecific immune response in chicks. [24] Similarly, Stresszee is also an herbal antioxidant, anti-stressor and adaptogen having the extracts of herbal plants such as *Ocimum sanctum* and *Withania somnifera*

Tinospora cordifolia- It is known to have shown effect on diabetes in rats. Asparagus racemosus has shown antioxidant properties against damage induced by gamma radiation and development of intraperitoneal adhesions and macrophage modulation in animal models. Not only they strengthen the defense mechanisms against free radical damage during stress conditions they also induce immunostimulation. The *Ocimum sanctum* seed oil has been found to contain significant antioxidant and chemopreventive properties against 20-Methylcholanthrene induced fibrosarcoma in mice.

Keeping the indispensable use of herbs as modifiers of immune system particularly anti stressor properties, the systematic and in-depth research is required in exploring the potential of herbal immunomodulators and to elucidate their mechanism of action.

Market name of herbal immunomodulator	Constituents	Indications	Animals
Stresszee or Zeetress	WS and OS	Antistressor and adaptogen	Broilers , turkeys, pigs, equine,camels, dogs and cats
Immuplus	WS, TS, OS, EO	Antistressor, weight gain in poultry birds ,better immune competence	Broilers and pigs
Restobal	WS,OS,EO, Asparagus racemose	Anti stressor, immune competence	Camels,

Conflict of Interest: None

REFERENCES

1. R Agarwal, S Diwanay, P Patki et al. Studies on immunomodulatory activity of Withania somnifera (Ashwagandha) extracts in experimental immune inflammation. J Ethnopharmacol. 1999; 67 (1): 27–35.
2. R Archana, A Namasivayam. The effect of acute noise stress on neutrophil functions. Indian J Physiol Pharmacol. 1999; 43 (4): 491–495.
3. A Bhattacharya, S Ghosal, SK Bhattacharya. Antioxidant effect of Withania somnifera glycowithanolides in chronic stress-induced perturbations of oxidative free radical scavenging enzymes and lipid peroxidation in rat frontal cortex and striatum. J. Ethnopharmacol. 2001; 74: 1–6.
4. MK Al Hindawi, IH Al Deen, MH Nabi et al. Anti inflammatory activity of some Iraqi plants using intact rats. J Ethnopharmacol. 1989; 26 (2):163–168.
5. M Ziauddin, Neeta Phansalkar, Pralhad Patki et al. Studies on the Immunomodulatory effects of Ashwagandha. J Ethnopharmacol. 1996; 50 (2): 69–76.
6. S Arora, S Dhillon, G Rani et al. The in vitro antibacterial synergistic activities of Withania somnifera extracts. Fitoterapia. 2004; 75 (3-4) 385–388.
7. RK Kath, RK Gupta. Antioxidant activity of hydroalcoholic leaf extract of Ocimum sanctum in animal models of peptic ulcer. Indian J Physiol Pharmacol. 2006; 50 (4): 391-396.
8. R Kath, R Gupta. Effect Of Ocimum Sanctum Leaf Extract On Swimming Stress Induced Ulcers In Rats. The Internet Journal of Third World Medicine. 2012; 10 (1)
9. P Dharmani, VK Kuchibhotla, R Maurya et al. Evaluation of anti-ulcerogenic and ulcer-healing properties Of Ocimum sanctum Linn. J Ethnopharmacol. 2004; 93 (2-3): 197–206.
10. S Singh, DK Majumdar. Evaluation of the gastric antiulcer activity of fixed oil of Ocimum sanctum (Holy Basil). J Ethnopharmacol. 1999; 65 (1): 13 – 19.
11. RK Geetha, DM Vasudevan. Inhibition of lipid peroxidation by botanical extracts of Ocimum sanctum: in vivo and in vitro studies. Life Sci. 2004; 76 (1) 21–28.
12. A Kumar, R Shukla, P Singh et al. Chemical composition, antifungal and antiaflatoxigenic activities of Ocimum Sanctum L. essential oil and its safety assessment as plant based antimicrobial. Food Chem Toxicol. 2010; 48 (2): 539–543.
13. J Prakash, SK Gupta. Chemopreventive activity of Ocimum sanctum seed oil. J Ethnopharmacol. 2000; 72 (1-2): 29–34 .
14. S Sood, D Narang, MK Thomas et al. Effect of Ocimum sanctum Linn. on cardiac changes in rats subjected to chronic restraint stress. J Ethnopharmacol. 2006; 108 (3): 423–427
15. M Sharma, K Kishore, SK Gupta et al. Cardioprotective potential of Ocimum sanctum in isoproterenol induced myocardial infarction in rats. Mol Cell Biochem. 2001; 225 (1): 75–83.
16. S Sood, D Narang, AK Dinda et al. Chronic oral administration of Ocimum sanctum Linn. augments cardiac endogenous antioxidants and prevents isoproterenol-induced myocardial necrosis in rats. Journal of Pharmacy and Pharmacology. 2005; 57: 127–133.
17. R Archana, A Namasivayam. Antistressor effect of Withania somnifera. J Ethnopharmacol. 1999; 64 (1): 91–93.
18. R Archana, A Namasivayam. Effect of Ocimum sanctum on noise induced changes in neutrophil functions. J Ethnopharmacol. 2000; 73 (1-2): 81–85.
19. K Sembulingam, P Sembulingam, A Namasivayam. Effect of Ocimum sanctum Linn on the changes in central cholinergic system induced by acute noise stress. J Ethnopharmacol. 2005; 96 (3): 477–482.
20. K Sembulingam, P Sembulingam, A Namasivayam. Effect of Ocimum sanctum

Linn on noise induced changes in plasma corticosterone. Indian J Physiol Pharmacol. 1997; 41 (2): 139–143.
21. K Sembulingam, P Sembulingam, A Namasivayam. Anti-stressor effect of Ocimum sanctum linn on changes in organ weight of albino rats induced by acute noise stress. Biomedicine. 1998; 18: 31–35.
22. K Sembulingam, P Sembulingam, A Namasivayam. Effect of Ocimum sanctum linn on noise induced changes in leukocytes of albino rats. Indian J Physiol Pharmacol. 1999; 43: 137–140.
23. SG Mode, ST Funde, SP Waghmare et al. Effect of Herbal Immunodulator on Body weight gain in immunosuppressed broiler birds. Vet World. 2009; 2 (7): 269-270.
24. BS Dhote, GK Singh, RS Chauhan. Effect of immuplus (a herbal immunomodulator) on paraspecific immune responses in chicks. In XIIth International Congress in Animal Hygiene, 2005 Sep 4-8; Warszawa, Poland Warsaw Agricultural University, Warsaw, Poland

How to cite this article: Preeti Srivastava, Farah Naz Faridi, Mudit Sharma. Plant based immunomodulators for managing stress in animals- a review. *Int J Health Sci Res.* 2022; 12(11):179-183.
DOI: *https://doi.org/10.52403/ijhsr.20221122*

******