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Tinospora cordifolia: A review of its potential as a heat stress relieving phyto-feed supplement in animals

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ABSTRACT

Summers will become increasingly hot as a result of climate change, with temperatures rising above the thermoneutral range of animals, exposing them to heat stress. Oxidative stress, which is caused by an increase in reactive oxygen species, is one of the most dangerous side effects of long-term heat stress. In order to alleviate oxidative stress, metabolites required for living and development may be depleted, which can have a negative impact on animals' growth and production performances, especially in chronic situations. Plant-derived phyto-feed additives with greater antioxidant quantity may benefit animals by lowering the effects of heat stress-induced oxidative stress. Improved pharmacological response and lack of adverse impact when compared to allopathic medications, phyto additives of curative benefit are becoming more frequent in medical research. *Tinospora cordifolia* is a popular term recognized as "Guduchi" or "Giloy" for its use in the treatment of different illness in naturopathic texts from the past. The bioactive components recovered from the plant, as well as its significance in prevention of illness, have helped the herbs to play a more active role in the field. It has antioxidant potential and can be exploited as a dietary additive to provide antioxidants for health benefits. The plant's common name, chemical components found in various portions of the plant, and biological functions are all covered in this review. In addition, they have potential as heat stress relievers in animals.

Keywords: *Tinospora cordifolia*, Diseases, Giloy, Heat Stress.

INTRODUCTION

Stress is characterized as the cumulative harmful effect on animal health and performance of a range of factors [1]. Physical, nutritional, physiological, psychological, and heat stress are only some of the stressors that animals face. In all this, heat stress is the indeed terrible concern today in the constantly-changing environment development [2], and it is among the utmost serious stressors particularly in the tropics and subtropics weather [3], dry [4] and semi-dry [5] areas of the world. 20-30 per cent of livestock are predicted to be at risk of survival [6] owing to the change in environment and weather variability. Climate change and rising ambient temperatures have been observed in many places, and extreme heat is becoming an issue in both hot and temperate settings [7]. Global warming in the farming of livestock has a broad economic significance which disturbs reproductive and productive output, including the quality of the commodity generated such as meat, milk and hair. Temperature and humidity put directly stress on these animals, particularly during grazing in pastures or field conditions. In the framework of the scant knowledge accessible to domesticated ruminant animals, heat stress affects maturation of ovaries and fetal growth, resulting in diminished fertility. Heat stress reduces animal development, fertility, productivity, and well-being by consolidating body reserve such as proteins and energy. [8]. Besides, heat stress affected quality and quality of milk [9]. Natural homeostatic adjustments to heat stress in animals include enhanced breathing, body temperature [10], reduced water retention, decreased appetite, rumination period and intake of dry matter [11]. Heat stress also reduces natural immunity and makes animals more susceptible to disease and even death will occur if the amount of heat sensed by the animal is extreme [12]. Heat stress can exceed the free radicle formation (superoxide anion, hydroxyl radicals, peroxide radicles and singlet oxygen) that are produced endlessly during natural oxidizing metabolism. An effective method for mitigating the influence of heat stress on animals is to adjust the climate by using sheds, fans or evaporative cooling. In semi-intensive operations, these practices are not feasible, as animals are grazed openly for majority of the day. It compels other approaches to tackle heat stress ill effects such as antioxidant supplements. Antioxidants are scavengers of free radical that shield the body's defense mechanism from disproportionately created free radicals under heat stress and help to maintain the animal's health. Plants provide natural antioxidants in the form of phenolic chemicals for instance flavonoids, phenolic acids, and tocopherols [13]. Animal nutrition and livestock production issues can be addressed by using natural materials as phyto-feed additives as stress relievers. India has a wide assortment of plant species, many of which have been used as medical plants since ancient times. These plants provide a variety of natural substances and medicines. Giloy (*Tinospora cordifolia*) is one of the useful medicinal plants that can be consumed either raw or processed. It is used to treat a variety of

illnesses, including chronic illness, dengue infection (by boosting platelet tally), allergic rhinitis, virus diseases, blood sugar control, immunity boost, digestion improvement, stress and anxiety reduction, and more [14].

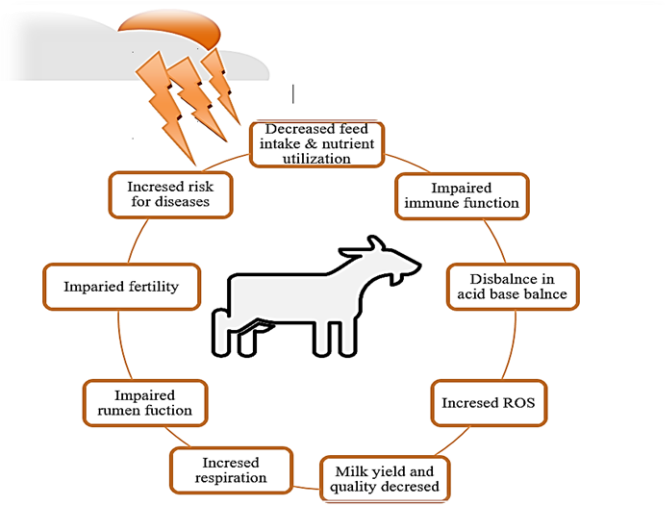

Figure 1: The impact of heat stress on animals

***Tinospora cordifolia* (Giloy)**

Tinospora cordifolia commonly referred to as Giloy in Hindi and Guduchi in Sanskrit is undoubtedly one of the most important versatile herbs found in India. It is a robust, deciduous climbing shrub with typical greenish-yellow blooms that bloom at higher elevations [15]. In addition to plains, the plant can also be found in the Himalayas, where it can be found at a height of around 1000 feet, and it can be found across a magnanimous zone of India, from the Kumaon Mountains in the north to Kanyakumari in the south. It can also be found in Asia, such as China, Sri Lanka, Thailand, the Philippines, and Malaysia, as well as Africa [16]**.** Although every part of the plant has therapeutic value, the stem is the most utilized component. It confines an array of active constituents that may have an effect on the body. Some of these active substances have antioxidant properties, while others may stimulate the body's immunological system [15].

a) Leaf

b) Stem

c) Seed

Figure 2: *T. cordifolia;*

In the customary Indian medicinal system, *T. cordifolia* has been recognized as the most widely used plant ever and exhibited countless promising biological functions such as antioxidative, anti-inflammatory, chemo preventive, radioprotective, neuroprotective, hypolipidemic, anti-allergic rhinitis, hepatoprotective, anti-ulcer, cardioprotective, hypoglycemic anti stressor and immunomodulatory impact [17]. Its root has antimalarial and stress-relieving qualities, but its stem is bitter and diuretic [18].

Bioactive substances and phytochemistry

Several phytochemicals, including as alkaloids, diterpenoid, glycosides, and polysaccharides, have been well reported from various portions of the plant. Some of the principal phytochemicals derived from the plant are tinosporine, tinosporide, tinosporaside, cordifolide, cordifol, heptacosanol, clerodane, diterpenoid, tinosporidine, columbin, and b-sitosterol. The plant's stem has been displayed to contain berberine, palmatine, tembertarine, magniflorine, choline, and tinosporin. Phenolics, flavonoids, proanthocyanidin and anthocyanidin contents in different powdered extracts of *T. cordifolia* stem by using HPLC method identified [19]. *T. cordifolia* stems had a overall phenolic substance of 12.8 mg/gm [20]. Natural products are

increasingly being used as feed additives to alleviate animal nutrition and animal production difficulties. Animal digestibility, feed conversion ratio, quality carcass meat, and safety have all been described to better with the application of phytogenic feed additives [21]. Plant secondary metabolites are an important area of contemporary research in the exploration of substitutes for chemical feed additives. Free radical scavenging function of *T. Codifolia* was excellent, and this plant needs more study [22].

Nutritional composition

T. cordifolia has the ability to provide nutrients and minerals to both humans and animals. It has a rich fiber content (15.9 per cent), a decent crude protein (4.5 -11.2 per cent), a high carb content (61.66 per cent), and a minimal fat content (3.1 per cent). It has a caloric value of 292.54 per 100g. It contains a lot of potassium (0.845 per cent), rich in chromium (0.006%), iron (0.28%) and calcium (0.131%), which are all crucial for various regulatory functions. [23]. *T. cordifolia's* stem has a low water content (34.39 per cent) and a significant amount of crude fibre, as per proximate study (56.42 per cent). Other components identified in low concentrations include protein (7.74 pe rcent), ether extract (0.912 per cent), total ash (7.96 per cent), and others. Calcium has the highest proportion (102.233 ppm), followed by iron (26.058 ppm) and phosphorous (102.233 ppm) (24.816 ppm). Other trace elements, such as manganese (12.242 ppm), zinc (7.342 ppm), and copper (3.733 ppm), are present in trace amount [24].

Table 1: Chemical components of *T. cordifolia* [25]

Plant part	*Name of chemical*
Whole plant	Diterpenoid lactones -Clerodane derivatives, tinosporon, tinosporides, jaiterine, columbin Aliphatic compounds -Octacosanol, heptacosanol nonacosan-15-one Flavonoids, glycosides, phenols, tannins, saponins and alkaloids Compound TC-1 (alkaloid) Tannins, steroids, flavonoids, cardiac glycosides and saponins Alkaloids, flavonoids, Saponin, tannins, steroidal terpenes, reducing sugar Alkaloids, tannins, cardiac glycosides, flavonoids, saponins and steroids
Stem	Alkaloids -Berberine, Tembeterine Glycosides -18-norclerodane glucoside, furanoid diterpene glucoside, cordiofolioside A, cordiofoliosideB, palmatosides C, palmatosides P1, Cordiofolioside C, cordiofolioside D, cordiofolioside E Sesquiterpenoids –Tinocordifolin Steroids -Sitosterol, 20 -hydroxy ecdysone, makisterone, giloinstero Isoquinoline alkaloid. Active compounds [(5R, 10R)-4R, 8R-Dihydroxy-2S, 3R:15, 16-diepoxycleroda-13(16), 17, 12S, 18, 1S-dilactone]
Leaves	Compounds identified in essential oil include alcohols (32.1%), phenols (16.6%), aldehydes (16.2%), fatty acids (15.7%), alkanes (8.3%), esters (3.2%), terpenes (1.2%), major compounds hydroquinone (16.6%), 2-hexenal (14.2%), palmitic acid (14.1%), 2-hexen-1-ol (11.5%) and phytol (11.4%).
Root	Alkaloids -Choline, Tinosporin, isocolumbin tetrahydropalmitine, jatrorrhizine Miscellaneous compounds- Tinosporidine, cordifol, cordifelone, N-trans-feruloyl, tyramine as diacetate, giloin, tinosporic acid

Antioxidant activity

Antioxidants are those phytochemicals that balance the oxidative stress effect by counteracting the reactive oxygen species (ROS), reactive nitrogen species (RNS), reactive sulfur species (RSS) and additional oxidant forming elements, in the animal body through various stressors, disease/syndrome conditions. In the past two decades, plant-extracted antioxidants are the utmost centered exploration areas by researchers since these antioxidants are more competent and harmless in contrast to chemically obtained antioxidants. *T.* cordifolia provide a rich supply of natural antioxidants, such as phenolic substances and flavonoids are widely distributed in the plant kingdom. Owing to their powerful antioxidant potential plant polyphenols have attracted researchers to their mark effect against various oxidative stress. *T. cordifolia* could inactivate free radicals generated during aflatoxicosis [26]. *T. cordifolia's* intended and unintended antioxidant effects are likely to work in tandem to produce the overall radioprotective effect [27]. The six weeks treatment of *T. cordifolia* stems methanolic extract (500mg/kg body weight) was evidenced antioxidant present in the plant as the action of plasma lipid peroxide and catalase (CAT) was effectively reduced, whilst superoxide dismutase (SOD) and glutathione peroxidase (GHS-Px) were substantially increased when compared to diabetic rats [28]. The *in vitro* study showed that the extract of *T. cordifolia* has a varied scale of antioxidant as well as antimicrobial activity against bacterial as well as fungal pathogens [29]. Total phenolic amount of stem of *T. cordifolia* was 66.28 ± 0.82 mg TA/g of ethanolic extract and 51.86±0.77 mg TA/g of methanolic extract and the antioxidant potential of the methanolic extract was limited in contrast to the ethanolic extract [30]. *In vitro*, stem extract (50-500 g) reduced the production of superoxide and hydroxyl radicals in both enzymic and non-enzymic modes [31]. The outcomes of this study support the notion that *T. Cordifolia* is a stellar resource of antioxidants and call for additional research into this plant.

Antistress activity

During the summer, when the ambient temperature rises high, the animals suffer from hyperthermia and heat stress (oxidative stress) due to incessant exposure to solar radiation on the range, which stimulates the production of large quantities of reactive oxygen species. The root *T. Cordifolia* is historically considered to be used for its anti-stress behaviors. Oral administration of *T. cordifolia* plant powder orally @ 500mg/kg BW for 30 days in solar-induced heat stress in goats maintained under different management system significantly reduced heat stress [32]. Ethanol extracts of *T. cordifolia* at 100 mg/kg unveiled noteworthy antistress potential in all the measures assessed, compared with diazepam at 2.5 mg/kg [33]. *T. cordifolia's* immunostimulant action could regulate the psychoneuroendocrine axis and provide resilience against diverse stressors [34]. Multiple research findings reported a decline in the stress-induced upsurge in serum corticosterone levels. These positive benefits may be mediated by modes such as oxidative stress injury prevention and cytokine modulation [35]. In a series of study, *T. cordifolia* and *Centella asiatica* were assessed for potential anti-stress activity. *T. cordifolia* showed significant protection against Cd-induced oxidative stress in the liver of rat [36]. Dietary addition of the assessed polyherbal mixture has some positive outcomes on immunological measures in stressed hens equivalent with those achieved [37].

Immunomodulatory activity

Administration of methanolic extract of *T. cordifolia* stem in mice found increased white blood cells significantly and humoral immune reaction [38]. The aqueous stem extract of *T. cordifolia* enhances secretion of macrophagic NO in a dose-reliant way in the occurrence of LPS that help in destroying tumor cell and immunostimulation with the secretion of IL-6 which plays a critical function in the stimulus of B-cell proliferation [39]. Polysaccharide G1-4A from *T. cordifolia* induced proliferation activity of B-cell and degeneration of IkB-α as well as LPS are impeded by TLR4-MD2 antibody which denotes that G1-4A bound to the TLR-4 receptor on the surface of B cell, trigger the NF-kB and regulate gene expression, cytokine synthesis and propagation of B cell [40]. Scientific studies have shown giloy to possess the properties like anthelminthic, anti-inflammatory, aphrodisiac, hepatoprotective, brain tonic, blood purifier, immunomodulatory, antineoplastic, antioxidant, antituberculosis, antipyretic, anti-osteoporotic, allergic treatments and adverse reaction restraint of the cancer therapy [41]. It strengthens the immunity of the body by increasing cytotoxic T cells and B cells differentiation, enhance antibody formation therefore, this rejuvenating herb is used as an important ingredient in 'Chyawanprash'. The anti-HIV activity of root extract revealed a reduction in the eosinophil count and facilitate of B lymphocytes and macrophages [42]. *T. cordifolia* aqueous extract (AETC) therapy promoted leukocyte regaining in cyclophosphamide-injected mice, and AETC therapy of macrophages resulted in better IFN-, TNF-, and IL-1 expression and *C. albicans* infested mice treated with AETC at the concentration of had survivability of 40% and 60%, respectively, while mice treated with fluconazole at a dose of 50 mg/kg had a survivability of 20%, curiously, mice are infected with C. albicans after AETC treatment showed improvement in the organ indices and liver function [43]. The oral treatments of *T. cordifolia* aqueous extract to birds at 10 ml per day per head (one day old to four weeks of age) group exhibited substantial surges of IL-2, IFN-γ, IL-4 and IL-1β expressions in chicken assessed to the control groups experimentally infected with very virulent IBDV [44]. *T. cordifoliais* reported benefiting the immune system in a sort of ways [45]. The TC-1, TC-2, TC-4, TC-5, TC-6 and TC-7 compounds exhibited enhanced IgG antibodies [46]. Into an *in vitro* slide technique of phagocytosis, *T. cordifolia* extracts were competent to induce polymorphonuclear cells for phagocytosis of added candida cells [47]. Aqueous *Tinospora* extracts have been also postulated to impact the cytokine formation, mitogenicity, stimulus and initiation of immune effector cells [48]. The stem extract of *T. cordifolia* was screened for antibacterial activity and was found to have so against pathogenic strains [49]. Studies carried out on the herbs such as *W. somnifera, T. cordifolia* and *A. indica* against chicken infectious anemia an immunosuppressive viral sickness of young chicks for immunomodulatory potential, unveiled that these herbs have the exceptional ability in encouraging both the cellular and humoral immune responses in chicks against the pathogenic virus and also restoring consequences of viral pathogenesis were noticed [50]. *T. cordifolia* (stem) shows potent immunomodulatory action [51]. The water and ethanol extracts of stems of *T. cordifolia* and *T. sinensis* hamper immunosuppression caused by cyclophosphamide [52].

CONCLUSION

T. Cordifolia is a well-known plant used in ancient Indian remedy to treat a range of ailments. It could supress free radicals and block free radicals, prevent radical-induced damage to the membrane and has the properties of immunomodulation. It is an exceptional medication that has the potential to be a valuable remedy for numerous animal and human complications but the protection and possible indications in humans and animals need to be identified. It is a significant source of nutrients, micronutrients and some important microelements. The current review article now emphasizes its prospect as an herbal feed supplement to fight stress and immunomodulation of animals.

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