



# Phytoimmunomodulators - Approach towards Potentiating Immunity of Cows during Transition period - A Review

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## Abstract

*Transition from gestation to lactation accounts for great metabolic stress to dairy cows. During this period, many components of host defense system are altered viz. function of neutrophils, stimulation and responsiveness of lymphocytes to mitogens, response of antibodies and production of cytokine by immune cells. Strengthening the non-specific immunity by reducing the stress of cow is the only perspective to overcome the incidence of diseases during this period. Many plants have eminent antioxidant potential. Few of them have been identified and tested by modern scientific methodologies for their in-vitro antioxidant potential e.g. Ocimum sanctum, Syzygium aromaticum, Emblica officinalis, Asparagus recemosus, Cinnamomum zeylanicum, Nigella sativa, Tribulus terrestris, Tinospora cordifolia and Withania somnifera etc. They are used in animal and human medication throughout history. The literature reveals that these natural antioxidants represent a potential side effect-free alternative. They have range of biochemical activities like, inhibiting the generation of reactive oxygen species (ROS), free radical scavenging activity either directly or indirectly as well as alteration of redox potential at intracellular level. They may be one of the promising option during this period. Such an alternative towards potentiating immunity reduces the problem of antibiotic resistance, drug residue and also ensure general wellbeing and functional life of cows.*

**Keywords:** Cow, Immunity, Phytoimmunomodulators, Stress, Transition Period.

## Introduction

Oxidative stress (OS) is considered as the primary cause of numerous stresses during transition cow. During transition period animal suffers from severe negative energy balance. It can be estimated through high concentration of non-esterified fatty acids (NEFA) and reduced plasma or serum concentrations of several vitamins and minerals in blood. Cumulative effect of all these changes is suggestive of lowered health status (Goff, 2006). During this period cow's metabolism shifts from demand of pregnancy to those of lactation. It leads to chain of biochemical and physiological reactions mainly, augmented production of ROS and ultimately immunosuppression (Sordillo, 2005). Especially immune cells have greater sensitivity to oxidative stress since (1) amount of polyunsaturated fatty acids on their membranes is very high which make them susceptible to peroxidation (2) After stimulation they produce large amount of ROS. Increased challenge to pathogenic microorganisms and decreased animal resistance renders animal more susceptible to various infectious and non-infectious diseases during this period (Goff, 2000). High incidence of disease during this period is major cause of concern for the dairy farmers. For combating these diseases chemotherapeutics is practiced since many years but it has lot of disadvantages *i.e.* expenditure on treatment, drug resistance in animal and also the human health hazard due to consumption of contaminated final product. Therefore, as a preventive measure we need to adopt proper managemental strategy. In order to strengthen this strategy literature regarding *in-vitro* antioxidant potential of these herbs, associated immunological changes as well as problems related to them and a prospective managemental innovation by the supplementation of phytoimmunomodulators during transition period is briefly reviewed.

## Changes During Transition Period

When cow attain full term of pregnancy, feto-maternal axis gets activated and cow started suffering from stress of parturition which ultimately leads to high rise in cortisol (Erskine, 2001). Although high plasma levels of cortisol mediate parturition reflex. But at the same time, cortisol binds to receptors present on the surface of neutrophils and subsequently reduces their ability to kill the foreign microbes (Burton *et al.*, 2005) which renders the animal more susceptible to infectious diseases. Hence, we can say that level of cortisol is also indicative of phagocytic activity of poly-morphonuclear neutrophils which is one of the predominant immune cell present in the bovine blood and act as first line of defence for any foreign material. Previous reports available which shows that, reported, decreased ability of neutrophils to ingest and kill the bacteria during first week of lactation (Kehrli *et al.*, 2006). Basically neutrophil is a phagocytic granulocyte. Myeloperoxidase is necessary enzyme for neutrophil to effectively destroy the bacteria that it has engulfed. Plasma NEFA level increases during transition period, the ability of neutrophil to produce myeloperoxidase is decreased (Corbett, 2009). This mechanism further reduced the capacity of immune cells to kill the microbes. Simultaneously, a number of immunophysiological alterations are induced in the dam body that lead peripartum susceptibility to immune-compromised disorders like mastitis, metritis, retention of foetal membrane and lower utero-cervical disorders *etc* (Beagley *et al.*, 2010).

## Herbs Used as Immunomodulators

Phytoimmunomodulators, commonly known as immunomodulating compounds of herbal origin, have well defined role on immune system. Actually immunomodulators modulate the immune system in negative as well as positive way. Positive impact of phytoimmunomodulator is that, they help in reducing stress and subsequently enhance resistance for combating infections (Rochfort *et al.*, 2008). They are widely used as nutrient for ruminant ration. Since they have antimicrobial activity which improve fermentation efficiency of rumen as well as mitigate emission of methane gas (Khiaosa-ard and Zebeli, 2013). Apart from their antimicrobial activity, a number of laboratory researches have shown that aqueous as well as alcoholic herbal extract of these herbs have strong anti-inflammatory and antioxidant properties. Few active antioxidant components present in the herbs are 6-gingerol, 6-shogaol, caffeic acid, carnosic acid, carnosol, carvacrol, eugenol, ferulic acid, rosmarinic acid, saponin and vanillin *etc*. The antioxidant activity of these plant extracts are estimated in laboratory several times with the help of 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, Ferric ion Reducing Antioxidant Power (FRAP) assay and total flavonoid content. In this paper these important herbs are discussed with their immunomodulatory action *in-vivo* as well as *in-vitro*. These results can be utilized for combating immunosuppression during advance pregnancy.

### *Ocimum sanctum*

**Family:** Lamiaceae

**Common name:** Tulsi

**Active principal:**  $\beta$ -careophyllin, Carvacrol, Eugenol, Oleonic acid, Rosmarinic acid and Ursolic acid.

Ayurveda always focuses on the use of herbs. One of the most important herb principally used in the Ayurveda is Tulsi (*Ocimum sanctum* Linn). Due to its multifactorial effects it is also regarded as mother medicine of nature. *Ocimum sanctum* is potent antioxidant. Several *in-vivo* and *in-vitro* studies indicate that essential oils present in *Ocimum sanctum* provide protection against injuries induced by toxic chemicals through augmenting the concentration of anti-oxidant molecules present in the body such as glutathione as well as augmenting the anti-oxidant enzymatic activity viz. catalase and superoxide dismutase, which protect cellular membranes and intracellular organelles by reducing the oxygen level and subsequently the free radical generation (Panda and Naik, 2009) and other toxic substances (Shivananjappa and Joshi, 2012; Manikandan *et al.*, 2007).

Alcoholic and aqueous extract of *Ocimum sanctum* at very low concentrations also have *in-vitro* anti-lipid peroxidase activity. Results of systemic studies which are designed to substantiate therapeutic claim pertaining to its clinical utility have shown that alcoholic as well as aqueous extracts of *Ocimum sanctum* has marginal stimulatory effect on humoral immunity (Vaghasiya *et al.*, 2010). In addition to antioxidant activity, *Ocimum sanctum* has immunostimulating potential which is helpful in treatment of immunosuppression. Essential oil present in the *Ocimum sanctum* enhance the production of IFN- $\gamma$ , IL-4, NK cells and T helper cells. Through this way it shows its immunomodulatory effect in the animal body (Mondal *et al.*, 2011). It also helps in raising neutrophil, lymphocyte count as well as improving phagocytic activity and phagocytic index by reducing total bacterial count. Essential oil extracted from *Ocimum sanctum* seed can mediate GABAergic pathways (Mediratta *et al.*, 2002). By this it can modulate both humoral and cell-mediated immunity. The fixed oil present in *Ocimum sanctum* is rich linoleic acid which could contribute towards its antibacterial activity. Some workers concluded from their study that fixed oil extracted from *Ocimum sanctum* showed excellent antibacterial activity against *Bacillus pumilus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* (Singh *et al.*, 2005). Out of which *Staphylococcus aureus* was the most sensitive to essential oil extracted from *Ocimum sanctum*. In addition to antibacterial activity, anti-inflammatory as well as analgesic properties *Ocimum sanctum* oil is also helpful in combating inflammatory disorders of *Staphylococcal spp.* origin.

It is also reported that aqueous extract of *Ocimum sanctum* lessen the total bacterial count by increasing lymphocyte and neutrophil count with enhanced phagocytic index, lysosomal enzymes contents of milk polymorphonuclear cells (Mukherjee *et al.*, 2005). The result suggests that the crude aqueous extract of *Ocimum sanctum* leaf possess some biologically active principles that are antibacterial and immunomodulatory in nature. Intramammary infusion of aqueous extract of *Ocimum sanctum* reduced the SCC and total bacterial count of *Staphylococcus aureus* significantly ( $P < 0.05$ ) in animals infected with subclinical mastitis (Mukherjee, 2006). When efficacy of fixed oil of *Ocimum sanctum* was compared alone and in combination with cloxacillin sodium during mastitis in buffaloes and reported comparable results with the standard drug (cloxacillin sodium-‘Floclox-L’) injection used during mastitis (Surender *et al.*, 1995). A cure rate of 100% was over 3-5 days’ period on the basis of quarters treated by intra mammary injection of 3 ml of *Ocimum sanctum* fixed oil alone as well as in combination with 200 mg of cloxacillin sodium. At the day of parturition FRAP assay of plasma is significantly ( $P < 0.05$ ) higher whereas least reduction in neutrophil phagocytic activity was observed in the crossbred dairy cows supplemented with poly-herbal mixture containing 19% *Ocimum sanctum* leaves and seeds @ 250 mg/kg body weight. However, 15 days’ postpartum mean Ig-G concentration in plasma was also significantly ( $P < 0.05$ ) more in crossbred dairy cows supplemented with poly-herbal mixture @ 250 mg/kg body weight as well as FRAP assay of plasma was also significantly ( $P < 0.05$ ) higher in crossbred dairy cows supplemented with poly-herbal mixture @ 200 mg/kg body weight (Sharma *et al.*, 2014). All these results represent the better antioxidant status of cows in poly-herbal mixture supplemented group during transition period. Decreased Ig-G level in plasma around parturition is associated with stress induced depression in lymphocyte activity. However, as compared to un-supplemented group, greater concentration of Ig-G was observed in group supplemented with 250 mg/kg body weight poly-herbal mixture. It is also suggestive of their higher B-lymphocytes activity due to better antioxidant status.

***Syzygium aromaticum***

**Family:** Myrtaceae

**Common name:** Clove

**Active principal:**  $\alpha$  and  $\beta$ -Caryophyllene, Eugenol, Eugenol acetate.

Several *in-vitro* studies indicated that *Syzygium aromaticum* has highest antioxidant potential among all the herbs. This is primarily due to the presence of eugenol. Hossain *et al.* (2011) tested 30 spices for their antioxidant potential using 2,2'-azinobis(3-ethylbenzothiaziline-6-sulfonate) (ABTS), FRAP and microsomal lipid peroxidation (MLP) assays and found that eugenol from clove had highest antioxidant capacity. In spite of antioxidant potential, eugenol also contributed to anti-inflammatory activity primarily by quashing the nuclear factor- $\kappa$ B pathway. Eugenol in non-cytotoxic concentrations also exert immunomodulatory action through augmenting the production of cytokine by murine macrophages (Bachiega *et al.*, 2012). Some descriptions are available regarding *Syzygium aromaticum* oil which show that it can enhance the immune response by augmenting humoral immunity and decreasing cell mediated immunity (Halder *et al.*, 2011). Literature reveals that supplementation of 185g phyto-biotic rich herbal mixture containing 4 % *Syzygium aromaticum* for 36 days resulted in reduced somatic cell score in the Holstein cows having high somatic cell count (Cigari *et al.*, 2014). It also represents reduced oxidative stress since both clinical and subclinical mastitis is associated with release of free radicals as well as total oxidative capacity (Atakisi *et al.*, 2010). It has been reported that immune response and immunity status are affected by the ingestion of antioxidant substances and oxidative stress (Grasso *et al.*, 1990; Politis *et al.*, 1995; Miyazaki *et al.*, 2001). *Syzygium aromaticum* feeding increase the antioxidant activity of the steer's plasma compared to the control group, which indicates that the antioxidant effect caused by clove feeding was not transient and was maintained for approximately a half day (Hosoda *et al.*, 2006). Therefore, *Syzygium aromaticum* is likely excellent among the herbs tested as a source of antioxidants for cattle and its ingestion may contribute to cattle health.

### ***Emblica officinalis***

**Family:** Phyllanthaceae

**Common name:** Amla/ Indian gooseberry

**Active principal:** Flavonoids, Kaempferol, Ellagic acid and Gallic acid.

In addition to high concentration of ascorbic acid, the fruits of *Emblica officinalis* contain phenols (ellagic acid, gallic acid, quercetin, kaempferol, corilagin, gnenin, furocin), tannins (gallotanins, emblicanins), flavanoids, glycosides and proanthocyanidines (Scartezzini and Speroni, 2000; Al-Rehaily *et al.*, 2002; Zhang *et al.*, 2001). The amount of phenols presents in the fruits and leaves of *Emblica officinalis* is similar while the roots of *Emblica officinalis* is rich in glycosides and tannins (Zhang *et al.*, 2001; Zhang *et al.*, 2000). Fresh fruit juice of *Emblica officinalis* is the rich source of ascorbic acid *i.e.* 1g/100ml and it account for 45% of antioxidant activity of *Emblica officinalis* (Scartezzini and Speroni, 2000). In addition to ascorbic acid, emblicans, gallic acid, methylegallate, corilagin, furocin, geranin and other compounds having antioxidant property (Kumaran and Kranukaran, 2006). *Emblica officinalis* also possess analgesic and antipyretic activity. Alcoholic and aqueous extracts of *Emblica officinalis* fruit showed analgesic and antipyretic activity in mice and the effect was comparable to aspirin (Mediratta *et al.*, 2002). In-vitro activity of alcoholic and aqueous extract of *Emblica officinalis* against certain dermatophytes and pathogen can commonly affect humans is suggestive of its anti-microbial property (Dutta *et al.*, 1998). It is that, at the day of parturition FRAP assay of plasma is significantly ( $P < 0.05$ ) higher and least reduction in neutrophil phagocytic activity in the crossbred dairy cows supplemented with poly-herbal mixture containing 19% dried *Emblica officinalis* fruit @ 250 mg/kg body weight. While 15 days after parturition mean Ig-G concentration in the plasma was also significantly ( $P < 0.05$ ) higher in crossbred dairy cows supplemented with poly-herbal mixture @ 250 mg/kg body weight as well as FRAP of plasma was also significantly ( $P < 0.05$ ) higher in crossbred dairy cows supplemented with 200 mg/kg body weight poly-herbal mixture containing 19% dried *Emblica officinalis* fruits which represents the better antioxidant status of cows in supplemented group during transition period. Reduced plasma Ig-G concentration around parturition might be due to stress which subsequently depress lymphocytic activity. However, as compared to un-supplemented crossbred cows, greater mean plasma Ig-G concentration was estimated in crossbred cows supplemented with poly-herbal mixture @ 250 mg/kg body weight. It is also suggestive of better antioxidant status as well as higher B-lymphocytic activity of cows in supplemented group.

### ***Cinnamomum zeylanicum***

**Family:** Lauraceae

**Common name:** Dalchini

**Active Principal:** Cinnamic acid, Cinnamaldehyde, Eugenol, Camphor, linalool and Trans-cinnamyl acetate.

In Ayurveda, *Cinnamomum zeylanicum* is regarded as remedy for digestive, gynecological and respiratory diseases. It comes under category of those plants whose every part has some medicinal value. A natural chemical compound

found in the bark of *Cinnamomum zeylanicum* trees is Cinnamonaldehyde whereas its root contain camphor. It has been reported that *Cinnamomum zeylanicum* extracts have significant inhibitory effects on *A. baumannii*, *E. cloacae*, *S. aureus* and *L. monocytogenes* at 0.4 mg/ml (Minimum inhibitory concentration) (Ahmad and Mehmood, 1998). Results of another study showed demonstrated that the essential oil of *Cinnamomum zeylanicum* exhibited robust antimicrobial activity against all microorganisms tested viz. *S. aureus*, *S. pyogenes*, *S. pneumonia*, *E. faecalis*, *E. faecium*, *B. cereus*, *A. lwoffii*, *E. aerogenes*, *E. coli*, *K. pneumoniae*, *P. mirabilis*, *P. aeruginosa*, *S. typhimurium*, *C. perfringens*, *L. monocytogenes*, *L. ivanovii*, *M. smegmatis*, *C. albicans*, *C. parapsilosis* and *C. krusei* (Bayoub *et al.*, 2010). Literature reveals that aqueous extract of cinnamon when included in the diet, subsequently improve antioxidant status of people suffering from obesity with impaired fasting glucose metabolism (Unlu *et al.*, 2010). Apart from that *Cinnamomum zeylanicum* also possesses anti-inflammatory and anti-carcinogenic effects (Roussel *et al.*, 2009; Ka *et al.*, 2003). It is also reported that phyto-biotic rich herbal mixture containing 18% *Cinnamomum zeylanicum* bark resulted in reduced somatic cell score when supplemented to the Holstein cows having high somatic cell count which is again suggestive of its better antioxidant potential (Cigari *et al.*, 2014).

### ***Asparagus racemosus***

**Family:** Asparagaceae

**Common name:** Shatavari/ Shatavar

**Active principal:** Saponins, Saponin

The genus *Asparagus* is rich source of saponins and saponin. Inouye *et al.*, 2001 reported that saponin is present in shatavari root. Besides saponin, root extract of Shatavari contain flavonoids (6.7±3.9 mg/100ml), polyphenol including tannin (88.2±9.3mg/100ml) and Vitamin-C (42.4±5.1mg/100ml) (Jadhav and Bhutani *et al.*, 2006). The presence of phyto-components in *Asparagus racemosus* root is phytoesters (0.79%), saponin (8.833%), polyphenols (1.692%), flavonoids (0.476%) and total ascorbic acid (0.762%) (Velavan *et al.*, 2007). It is described that supplementation of *Asparagus racemosus* root powder at 5 and 10% level reduces the plasma and hepatic lipid (cholesterol) levels as well as reduces lipid peroxidation (Visavadiya *et al.*, 2007). Mineral composition of Shatavari is Ca, Mg, K and Fe content 0.22, 0.4, 2.5, and 0.005g/100 g, respectively (Visavadiya *et al.*, 2005). Whereas micro-minerals Cu, Zn, Mn, Co and Cr were 5.29, 53.15, 19.98, 22.00 and 1.81 µg/g, respectively. High concentration of micro-minerals present in *Asparagus racemosus* is suggestive of its significant role in immunopotential. Feeding of *Asparagus racemosus* root induce leucocytosis besides predominant neutrophilia which might be associated with stimulation of bactericidal and phagocytic activity of neutrophils and macrophages (Chaudhari and Kar, 1992). At the day of parturition FRAP of plasma is significantly (P<0.05) higher, least reduction in neutrophil phagocytic activity in the crossbred dairy cows supplemented with poly-herbal mixture @ 250 mg/kg body weight containing 19% *Asparagus racemosus* root powder. Whereas 15 days' postpartum mean Ig-G concentration present in plasma was also significantly (P<0.05) high in crossbred cows supplemented with poly-herbal mixture @ 250 mg/kg body weight as well as FRAP of plasma was also significantly high in crossbred cows supplemented with poly-herbal mixture containing 19% *Asparagus racemosus* roots @ 200 mg/kg body weight which is representative of better antioxidant status of cows in supplemented group during transition period (Sharma *et al.*, 2014). Reduced Ig-G concentration in plasma around parturition might be suggestive of to stress associated lessening of lymphocyte activity. Although, in comparison to un-supplemented cows, greater Ig-G concentration in crossbred cows supplemented with poly-herbal mixture @ 250 mg/kg body weight. It is also reported that supplementation of *Asparagus racemosus* root powder @100mg/kg body weight from 60 before expected date of calving significantly (P<0.05) increased total immunoglobulin in colostrum (Thatte and Dhanukar, 1989).

### ***Withania somnifera***

**Family:** Solanaceae

**Common name:** Ashwagandha

**Active principal:** Steroidal alkaloid, Isopelletierine, Anaferrine, Withanoloid and Withaferin.

The biologically active compound present in *Withania somnifera* are alkaloids (isopelletierine, anaferrine), steroidal lactone (Withanolides, withaferins), saponin containing an additional acyl group (sitoinoside IX and X). Several studies revealed that *Withania somnifera* possess anti-inflammatory properties. Oral administration of powdered root (suspended in 2% gum acacia) at the rate of 1g/kg body weight in rat cause considerable reduction in Freud's complete adjuvant induced inflammation through significant decrease in acute phase plasma inflammatory proteins viz. alpha 2- glycoprotein, major acute phase alpha 1-protein and pre albumin (Kumar *et al.*, 2014).

The anti-inflammatory effect of *Withania somnifera* is comparable to steroidal anti-inflammatory agent. *Withania somnifera* also inhibited granuloma formation in cotton pelleted implantation in rats and effect was comparable to hydrocortisone sodium succinate (5mg/kg) (Anbalagan and Sadique, 1981). They suggested that anti-inflammatory property of *Withania somnifera* may be due to inhibition of cyclooxygenase enzyme.

*Withania somnifera* is well known for its anti-stress property. Anti-stress property of *Withania somnifera* is primarily due to presence of glycosides (sitoindosides VII and VIII). Since glycosides are potent antioxidants. Rats supplemented with *Withania somnifera* @ 50-100 mg/kg body weight, showed significant anti-stress ability during immobility induced by forced swimming, restraint induced auto analgesia in addition to, curb stress effect in response of toxicity induced by morphin (Al-Hindwani *et al.*, 1992).

Alcoholic extract of *Withania somnifera* (@ 100mg/kg, twice daily orally 1<sup>st</sup>, 4<sup>th</sup> or 7<sup>th</sup> day) reduced stress induced enhancement of blood urea nitrogen levels, blood lactic acid as well as adrenal hypertrophy (Bhattacharya *et al.*, 1987). However, it did not alter thymus weight in hyperglycemic rats. Immunomodulatory property of *Withania somnifera* can be attributed to glycowithanoloids and sitoindosides IX and X. These active principles produced statistically significant mobilization and induce activation of peritoneal macrophages, enhanced activity of lysosomal enzyme as well as phagocytosis in swiss mice and wistar strain albino rats (Dadgar *et al.*, 1987). Reports are available that at the day of parturition FRAP of plasma is significantly (P<0.05) high, least reduction in neutrophil phagocytic activity in the crossbred cows supplemented with poly-herbal mixture containing 19% *Withania somnifera* root @ 250 mg/kg body weight. At 15 days' postpartum mean Ig-G concentration in plasma was also significantly (P<0.05) higher in crossbred cows supplemented with poly-herbal mixture @ 250 mg/kg body weight. However, FRAP of plasma was also significantly (P<0.05) higher in crossbred cows supplemented with poly-herbal mixture containing 19% *Withania somnifera* root @ 200 mg/kg body weight which represents the better antioxidant status of cows in supplemented group during peripartum (Sharma *et al.*, 2014).

### ***Tinospora cordifolia***

**Family:** Menispermaceae

**Common name:** Giloy, Guduchi

**Active Principles:** 20  $\beta$ -hydroxy-ecdysone, inosporaside, cordioside and columbin.

The active principles of *Tinospora cordifolia* are 20  $\beta$ -hydroxy-ecdysone, inosporaside, cordioside and columbin (Ahamed *et al.*, 2006). *Tinospora cordifolia* poses antioxidant, hepatoprotective and immunostimulatory properties. Oral administration of aqueous root extract at the rate of 2.5 to 5 g/kg body weight for 6 weeks in alloxan diabetic rats decreased plasma thiobarbituric acid, reactive substances, ceruloplasmin and  $\alpha$ -tocopherol and increased glutathione and vitamin C concentration. The effect was more than glibenclamide (Prince and Menon, 1999).

*Tinospora cordifolia* caused significant reduction in serum SGOT, SGPT, ALP, bilirubin and increment in the functional capacities of rat peritoneal macrophages in carbon tetrachloride (CCl<sub>4</sub>) intoxicated mature rats. This indicates its hepatoprotective and immunostimulatory functions (Bishayi *et al.*, 2002). They also reported that an alcoholic extract of *Tinospora cordifolia* enhances the differentiation of tumour activated macrophages (TMA) to dendritic cells (DC) in response to granulocyte/ macrophage/ colony/ stimulating factors, interleukin-4 and tumor necrosis factor.

### ***Tribulus terrestris***

**Family:** Zygophyllaceae

**Common Name:** Gokhru, Puncture vine, Caltrop, Gokshura, and Chotagokhru.

**Active Principle:** Flavonoid glucosides.

The active principles in *Tribulus terrestris* are flavonoid glucosides. These mainly include flavonols, kaempferol, quercetin and isorhamnetin with the 3-gentiobiosides as the major glycosides (Saleh *et al.*, 1982).

Amin *et al.* (2006) studied the hepatoprotective effect of *Tribulus terrestris* in streptozotocin included diabetic rat and reported that oral administration of extract at the rate of 2g/kg body weight for 30 days, significantly (P<0.05) decreased serum ALT and creatinine and increase in liver GSH enzymes in diabetic rats. Histopathological examination revealed significant recovery of liver in herb treated rats. This investigation suggested the protective

effect in rats may be mediated by inhibiting oxidative stress.

Heidari *et al.* (2007) reported that soxhlet and percolated methanolic extract of *Tribulus terrestris* at the dose of 100 mg/kg produced significant analgesic effect in formalin and tail flick tests in rats. The analgesic effect of the extract was lower than morphine (2.5 mg/kg) in both tests and higher than aspirin (300 mg/kg) in chronic phase of pain in the formalin test ( $P < 0.05$ ). The results of ulcerogenic studies indicate that gastric ulcerogenicity of plant extract is lower than the indomethacin in the rat stomach.

Singh and Sisodia, (1972) reported that the extraction of *Tribulus terrestris* fruit powder with water removed the *Cucumis melo* (Musk melon) seed produced nephrotoxicity. The washed powder produced a decrease in urinary output, despite increased chloruresis.

*Tribulus terrestris* also possess anthelmintic property. Alcoholic extract and a mixture of crude alkaloids of the plant *Tribulus terrestris* inhibited the rate and force of contractions of *Ascaridia galli* in vitro, the effects being comparable to those produced by piperazine. The alcoholic extract and alkaloids also eliminated *A. galli* from chicken although they were less effective than piperazene at similar doses (Chakraborty *et al.*, 1979).

### ***Nigella sativa***

**Family:** Ranunculaceae

**Common Name:** Klonji, Black caraway, Black seed, Black cumin, fennel flower,

**Active Principle:** Thymoquinone, Dithymoquinone, Thymohydroquinone and Thymol.

Dadgar *et al.* (2006) reported that ethanolic extract of *Artemisia herba-alba*, *Nigella sativa*, *Punica granatum* possessed the most outstanding *in vitro* anti-bacterial activity with maximum inhibition zone of 22.4-18 mm. The lowest MIC value was measured in *Punica granatum* as 0.01 mg/ml against MRSA. The results showed that the aqueous extract and the MSRA was better than MSSA strains.

Tawab and Nasreen, (2006) treated Fe (III) solution with extract of *N. sativa* as well as two other active biological reductants, hydroquinone and hydroxyl ammonium chloride and found that *N. sativa* is stronger reducing agent than hydroxyl ammonium chloride and weaker than hydroquinone.

Treatment of rats with *N. sativa* inhibited ROS production induced by experimental auto immune encephalomyelitis (EAE) indicated by diminished levels of MDA of both brain and medulla spinalis tissues and NO brain only. When *N. sativa* was given alone to the rats, no changes were shown in brain, medulla spinalis and serum oxidant/antioxidant parameters. In conclusion *N. sativa* may protect brain and medulla spinalis tissues against oxidative stress induced by EAE. In addition, *N. sativa* display its antioxidant and regulatory effects via inflammatory cells rather than host tissue (brain and medulla spinalis) for EAE in rats (Ozugurlu *et al.*, 2005).

## **Conclusion**

Transition period is very stressful period in life of high yielding dairy cattle. In this period immune system of cow is in very suppressed state. This review was focussed on the fact that there several herbs around us which has potential to enhance immunity. These herbs are widely used in ethnomedicine since long back. An alternative approach towards potentiating the immune system of dairy animal with the use of these herbal ingredients can solve the problem of immunosuppression. This can ensure general wellbeing of cow and consequently will increase the functional life of cow. Only there is need to standardise their doses for boosting immune system of animals.

## **Contribution by Authors**

Each co-author contributes equally.

## **Conflict of Interests**

There is no conflict of interest.

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