

## Evaluation of Inflammatory Serum Cytokines after Treatment with the Consciousness Energy Healing Based Proprietary Test Formulation on Combination of Cecal Slurry, LPS and *E. Coli* Induced Systemic Inflammatory Response Syndrome (SIRS) in Sprague Dawley Rats

Mahendra Kumar Trivedi<sup>1</sup>, Alice Branton<sup>1</sup>, Dahryn Trivedi<sup>1</sup>, Snehasis Jana<sup>2,\*</sup>

<sup>1</sup>Trivedi Global, Inc., Henderson, Nevada, USA

<sup>2</sup>Trivedi Science Research Laboratory Pvt. Ltd., Thane (W), Maharashtra, India

### Corresponding author:

Snehasis Jana, Trivedi Science Research Laboratory Pvt. Ltd., Thane (W), Maharashtra, India

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### Abstract

Sepsis is a systemic inflammatory response to a confirmed or suspected infection. The transition from sepsis to septic shock causes high rate of mortality. The aim of this experiment was to

evaluate the anti-inflammatory potential of the Biofield Energy Treated (Blessed) Proprietary Test Formulation and Biofield Energy Healing (Blessing) Treatment *per se* to Sprague Dawley rats on Cecal Slurry, LPS, and *E. coli*-induced systemic inflammatory response syndrome (SIRS) model. In this experiment, various proinflammatory cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1 $\beta$  (IL-1 $\beta$ ), IL-6, IL-10, IL-12, 1L-17, and interferon- $\gamma$  (IFN- $\gamma$ ) were analysed using ELISA. A test formulation was formulated including minerals (magnesium, zinc, calcium, selenium, and iron), vitamins (ascorbic acid, pyridoxine HCl, vitamin E, cyanocobalamin, and cholecalciferol), *Panax ginseng* extract,  $\beta$ -carotene, and cannabidiol isolate. The constituents of the test formulation were divided into two parts; one section was defined as the untreated test formulation, while the other portion of the test formulation and three group of animals received Biofield Energy Healing Treatment remotely for about 3 minutes by a renowned Biofield Energy Healer Mr. Mahendra Kumar Trivedi. The level of TNF- $\alpha$  was significantly reduced by 40.50%, 85.36% ( $p \leq 0.01$ ), 50.66% ( $p \leq 0.01$ ), 87.38% ( $p \leq 0.01$ ), and 58.63% ( $p \leq 0.01$ ) in G5 (Cecal Slurry, LPS, and *E. coli* + Biofield Energy Treated test

formulation), G6 (Cecal Slurry, LPS, and *E. coli* + Biofield Energy Treatment *per se* to animals from day -15), G7 (Cecal Slurry, LPS, and *E. coli* + Biofield Energy Treated test formulation from day -15), G8 (Cecal Slurry, LPS, and *E. coli* + Biofield Energy Treatment *per se* + Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS, and *E. coli* + Biofield Energy Treatment *per se* animals + untreated test formulation) groups, respectively as compared to the disease control (G2) group. Additionally, the level of IL-1 $\beta$  was decreased by 17.04%, 15.56%, and 12.59% in G6, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group. The level of IL-6 was significantly ( $p \leq 0.001$ ) reduced by 36.18%, 50.24%, 43.25%, 52.69%, and 38.23% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the G2 group. The level of IL-10 was altered by 70.53%, 49.25%, 60.18%, 41.54%, and 58.89% in G5, G6, G7, G8, and G9 groups, respectively as compared to the G2 group. Moreover, the level of IL-12 was decreased by 30.24%, 31.67%, 29.82%, 45.77%, and 50.54% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the G2. The level of IL-17 was reduced by 48.75%, 59.61%, 59.28%, 62.49%, and 58.65% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the G2. IFN- $\gamma$  expression was reduced by 49.56%, 24.09%, 23.7%, 56.98%, and 44.94% in G5, G6, G7, G8, and G9 groups, respectively than G2. Overall, the data suggested anti-inflammatory potentials of the Biofield Energy Treated test formulation and Biofield Energy Treatment *per se* along with preventive measure on the animal with respect to various inflammatory conditions that might be beneficial various types of systemic inflammatory disorders specially sepsis, trauma, septic shock or any types of injuries. Therefore, the results showed the significant slowdown the inflammation-related disease progression and its complications in preventive treatment groups *viz.* G6, G7, G8, and G9.

## Introduction

Systemic inflammatory response syndrome (SIRS) is a complex pathophysiologic defense response of

the body to a noxious stressor such as infection, trauma, burns, pancreatitis, surgery, acute inflammation, ischemia or reperfusion, or malignancy or any others injuries [1, 2]. Sepsis is an infection which can considered a systemic inflammatory response. Clinically, the Systemic Inflammatory Response Syndrome (SIRS) is identified by two or more symptoms including fever or hypothermia, tachycardia, tachypnoea and change in blood leucocyte count [3]. Sepsis is a systemic inflammatory response to a confirmed or suspected infection. The development from sepsis to septic shock represents a continuum with increasing mortality. Research in the last two decades explored that the inflammatory process is play a major role in the mechanism of different vital systems pathologies [4]. Several cytokines (TNF- $\alpha$ , TGF- $\beta$ ) and interleukins (IL-1, IL-4, IL-6, IL-8, and IL-18) are responsible for the development of various inflammatory pathologies of various vital systems such as cardiac, renal, lymphatic, etc. [5]. Proinflammatory cytokines affect nearly all tissues and organ systems. A considerable research has been focused on the role of proinflammatory cytokines, interleukins, and tumor necrosis factor (TNF), in the pathogenesis of sepsis and septic shock associated with congestive heart failure [6]. The cytokine hypothesis has been proposed by scientists based on the idea that the activation of the inflammatory immune system, which specifically involved proinflammatory cytokines release, further stimulates various neurochemical and neuroendocrine changes [7]. Overall, cytokines role has been reported in various types of infections and the growth of malignant tumors, as the immune-stimulants and mediating the inflammatory response in a variety of human diseases [8, 9].

Thus, in order to study the change in serum cytokines in presence of Cecal Slurry, LPS and *E. coli*-induced systemic inflammatory response syndrome model in Sprague Dawley rats, a novel test formulation was designed with the combination of vital minerals (selenium, zinc, iron, calcium, and magnesium), essential vitamins (cyanocobalamin, ascorbic acid, pyridoxine HCl,

vitamin E, and cholecalciferol), and nutraceuticals ( $\beta$ -carotene, Ginseng, cannabidiol isolate (CBD)). All the minerals and vitamins used in the test formulation have significant functional role to provide vital physiological roles [10, 11]. Besides, cannabidiol itself has wide range of pharmacological profile and has been reported to role in different disorders [12, 13], while ginseng extract is regarded as the one of the best immune booster for overall immunity [14]. The present study was aimed to evaluate the anti-inflammatory potential of the Biofield Energy Treated Proprietary Test Formulation and Biofield Energy Treatment *per se* to the animals on Cecal Slurry, LPS and *E. coli*-induced systemic inflammatory response syndrome model in Sprague Dawley rats using serum biomarkers (cytokines).

Biofield Energy Healing Treatment has been reported with significant effects against various disorders, and defined as one of the best Complementary and Alternative Medicine (CAM) treatment approach [15-17]. National Center for Complementary/Alternative Medicine (NCCAM) recommended CAM with several clinical benefits as compared with the conventional treatment approach [18]. National Centre of Complementary and Integrative Health (NCCIH) accepted Biofield Energy Healing as a CAM health care approach in addition to other therapies such as deep breathing, natural products, Tai Chi, yoga, therapeutic touch, Johrei, Reiki, pranic healing, chiropractic/osteopathic manipulation, guided imagery, meditation, massage, homeopathy, hypnotherapy, special diets, relaxation techniques, movement therapy, mindfulness, Ayurvedic medicine, traditional Chinese herbs and medicines in biological systems [19,20]. The Trivedi Effect®-Consciousness Energy Healing was scientifically reported on various disciplines such as nutraceuticals [21], agriculture science [22], cardiac health [23], materials science [24, 25], antiaging [26], Gut health [27], pharmaceuticals [28], overall human health and wellness. In this study, the authors sought to study the impact of the Biofield Energy Treatment (the Trivedi Effect®) on the given novel test formulation and Biofield Energy

Treatment *per se* to the animals on serum cytokines in presence of Cecal Slurry, LPS and *E. coli*-induced systemic inflammatory response syndrome model in in Sprague Dawley Rats using standard ELISA assay.

## Material and Methods

### Chemicals and Reagents

Pyridoxine hydrochloride (vitamin B<sub>6</sub>), zinc chloride, magnesium (II) gluconate, and  $\beta$ -carotene (retinol, provit A) were purchased from TCI, Japan. Cyanocobalamin (vitamin B<sub>12</sub>), calcium chloride, vitamin E (Alpha-Tocopherol), cholecalciferol (vitamin D<sub>3</sub>), iron (II) sulfate, and Carboxymethyl Cellulose Sodium were procured from Sigma-Aldrich, USA. Ascorbic acid (vitamin C) and sodium selenate were obtained from Alfa Aesar, India. *Panax ginseng* extract and Cannabidiol Isolate were obtained from Panacea Phytoextracts, India and Standard Hemp Company, USA, respectively. Dexamethasone was obtained from Clear synth, India. For the estimation of serum inflammatory biomarker panel, cytokines estimation, specific ELISA kits were used such as for detection of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-10, IL-12, IL-17, and IFN- $\gamma$  were procured from CUSABIO, USA.

### Animal Welfare

All the animals were handled humanely with due regard for their welfare. The animal care were comply with the regulations of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Environment and Forest, Govt. of India. The test facility is registered (registration no. 64/PO/RcBi/S/99/CPCSEA) for experiments on animals with the CPCSEA. The animals were procured using the protocol approved (IAEC/42/533) by the Institutional Animal Ethics Committee (IAEC) and the husbandry conditions were maintained as per the recommendations of the CPCSEA.

### Maintenance of Animal

Randomly breed male Sprague Dawley (SD) rats with body weight ranges from 200 to 300 gm were used in this study. The animals were purchased from M/s. Vivo Bio Tech, Hyderabad, India. Animals were randomly

divided into nine groups based on their body weights consist of 10-12 animals of each group. They were kept individually in sterilized polypropylene cages with stainless steel top grill having provision for holding pellet feed and drinking water bottle fitted with stainless steel sipper tube. The animals were maintained as per standard protocol throughout the experiment.

#### *Consciousness Energy Healing Strategies*

Each ingredient of the novel test formulation was divided into two parts. One part of the test compound did not receive any sort of treatment and were defined as the untreated or control sample. The second part of the test formulation was treated with the Trivedi Effect® - Energy of Consciousness Healing Treatment (Biofield Energy Treatment) by a renowned Biofield Energy Healer, Mr. Mahendra Kumar Trivedi under laboratory conditions for ~3 minutes. Besides, three group of animals also received Biofield Energy Healing Treatment (known as the Trivedi Effect®) by Mr. Mahendra Kumar Trivedi under similar laboratory conditions for ~3 minutes. The Biofield Energy Healer was located in the USA, however the test formulation were located in the research laboratory of Dabur Research Foundation, New Delhi, India. The energy transmission/Blessing (prayer) was given remotely to the samples or animals for about 3 minutes *via* online web-conferencing platform. After that, the Biofield Energy Treated samples was kept in the similar sealed condition and used as per the study plan. In the same manner, the control test formulation group was subjected to “sham” healer for ~3 minutes treatment, under the same laboratory conditions. The “sham” healer did not has any knowledge about the Biofield Energy Treatment. The Biofield Energy Treated animals were also taken back to experimental room for further proceedings.

#### *Experimental Procedure*

Seven days after acclimatization, animals were randomized and grouped based on the body weight. The test formulation was prepared freshly prior to dosing

and administered to the animals using an oral intubation needle attached to an appropriately graduated disposable syringe. The dose volume was 10 mL/kg in morning and evening based on body weight. The experimental groups were divided as G1 as normal control (vehicle, 0.5% w/v CMC-Na); G2 as disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na); G3 as reference item (Cecal Slurry, LPS and *E. coli* + Dexamethasone); G4 includes Cecal Slurry, LPS and *E. coli* along with untreated test formulation; G5 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation; G6 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15; G7 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation from day -15; G8 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15, and G9 group denoted Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation. Dosing for groups G7 and G8 were started on Day -15 and continued till end of the experiment. However, Group G1 to G5 and G9 animals were dosed with respective formulations from Day 1 and continued till the end of the experiment. Group G6 animals received Biofield Energy Treatment on Day-15 and were not dosed throughout the experimental period. At the end of the experimental period (8 weeks treatment), the animals were sacrifice and blood was collected and separate serum subjected for cytokines (TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-10, IL-12, IL-17, and IFN- $\gamma$ ) estimation.

#### *Induction of Systemic Inflammatory Response Syndrome (SIRS) Model*

A combination model of sepsis was developed in SD rats by administering Cecal slurry (from donor animals, intraperitoneally, at the dose of 400 mg/kg) in combination with LPS (at the dose of 100  $\mu$ g/animal) and *E. coli* [*Escherichia coli*; 0.2 mL (2M CFU)/animal]]. The animals were monitored for various parameters for

up to 56 days after disease (SIRS) induction. Ten Donor (~20 weeks old) rats were anesthetized. A midline laparotomy was performed on them and the cecum was extruded. A 0.5 cm incision was made on the anti-mesenteric surface of the cecum, and the cecum was squeezed to expel the feces. The feces from different donor animals was collected and weighed. Immediately after collection, the feces were pooled, diluted 1:3 with 5% dextrose solution and filtered to get a homogeneous suspension. Bacterial viability in the cecal slurry was analyzed. Cecal slurry prepared from donor rats was injected intraperitoneally into experimental rats (G2 to G9) at the dose of 400 mg/kg within 2 hours of preparation. After 3 hours, lipopolysaccharide (LPS) at the dose of 100 µg/animal, and gram-negative viable bacteria such as *E. coli* [0.2 mL (2M CFU)/animal] were injected, intraperitoneally (G2 to G9).

#### *Mortality and Survival*

Animals were observed daily to check for SIRS related mortality. Mortality along with survival proportion across time was presented in Kaplan-Meier Graph. Percentage mortality, percentage survival and the increase in life span was calculated [29].

#### *Preparation of Sample for the Estimation of Cytokines*

With the continued treatment to the respective groups of 8<sup>th</sup> week of the experimental period, all the animals were individually subjected for blood collection using retro-orbital route and the blood was collected in the plain vial, which was used for the separation of serum in all the animals of different experimental groups. The serum from all the groups was stored at -20°C for further estimation. Alternatively, aliquot all the samples and store samples at -20°C or -80°C. Avoid repeated freeze-thaw cycles, which may alter the level of cytokines during final calculations.

#### *Estimation of Cytokine Levels*

The serum from all the groups was subjected for the estimation of level of cytokines such as TNF-α (CSB-E11987r), IL-1β (CSB-E08055r), IL-6

(CSB-E04640r), IL-10 (CSB-E04595r), IL-12 (CSB-E07364r), IL-17 (CSB-E07451r), and IFN-γ (CSB-E04579r). All the serum biomarker panel was estimation using ELISA method as per manufacturer's recommended standard procedure. This was a quantitative method and the principle was based on the binding of antigen and antibody in sandwich manner assay.

#### *Statistical Analysis*

The data were represented as mean (n=6 to 9) ± standard error of mean (SEM) and subjected to statistical analysis using Sigma-Plot statistical software (Version 11.0). For multiple comparison One-way analysis of variance (ANOVA) followed by post-hoc analysis by Dunnett's test and for between two groups comparison Student's *t*-test was performed. The  $p \leq 0.05$  was considered as statistically significant.

## **Results and Discussion**

#### *Mortality and Survival*

Mortality, particularly within a few hours/days of SIRS induction, was observed in all the disease induced groups, indicating the onset and severity of SIRS induction. The survival rates varied according to the treatment. A % increase in the proportion of surviving animals was observed in the groups G6, G7, and G8 when compared to disease control (G2) group, indicating an increased survival rate (Figure 1 and Table 1).

#### *Estimation of Serum TNF-α*

Serum cytokine, TNF-α was estimated in the presence of the effect of the test formulation, which was measured in all the experimental groups and was graphically presented in the Figure 2. The data suggested that the disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na) + 0.5% CMC group (G2) showed value of tumor necrosis factor-alpha (TNF-α) as  $32.68 \pm 5.71$  pg/mL, which was increased by 831.27% as compared with the normal control (G1,  $3.51 \pm 0.33$  pg/mL). However, positive control (Dexamethasone) treatment (G3) showed the level of serum TNF-α *i.e.*,  $12 \pm 2.4$  pg/mL, which was

Table 1. Mortality and Survival Data of Various Treatment Groups.

Group	Total No. of Animal	Total Mortality	Total Animals survived	% Survival Proportion	% Mortality
G1	10	0	10	100	0
G2	12	4	8	66.6	33.3
G3	12	3	9	75	25
G4	12	4	8	66.6	33.3
G5	12	4	8	66.6	33.3
G6	12	3	9	75	25
G7	12	3	9	75	25
G8	12	3	9	75	25
G9	12	4	8	66.6	33.3



Figure 1. Effect of Proprietary Product on Mortality and Survival (Kaplan Meier's Curve). BET: Biofield Energy Treatment/Blessing (prayer)

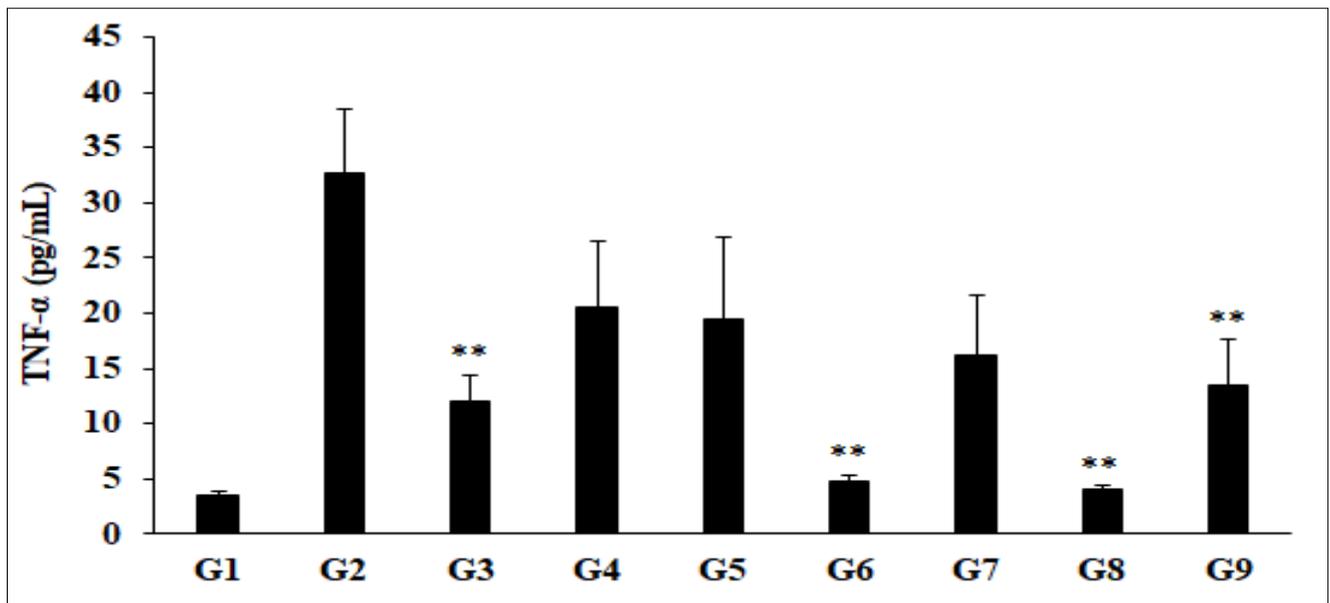


Figure 2. Expression the level of serum tumor necrosis factor-alpha (TNF- $\alpha$ ) after administration of Biofield Treated/Untreated proprietary test formulation and Biofield Energy Treatment *per se* to Sprague Dawley rats. The effect of the test formulation on the level of serum in Sprague Dawley rats. G1 as normal control (vehicle, 0.5% w/v CMC-Na); G2 as disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na); G3 as reference item (Cecal Slurry, LPS and *E. coli* + Dexamethasone); G4 includes Cecal Slurry, LPS and *E. coli* along with untreated test formulation; G5 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation; G6 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15; G7 as Cecal Slurry, LPS and *E. coli* + Biofield Energy Treated test formulation from day -15; G8 group includes Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15, and G9 group denoted Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* animals + untreated test formulation. Values are presented as mean  $\pm$  SEM (n=6-9). \*\* $p \leq 0.01$  vs. Disease control (G2) group.

significantly ( $p \leq 0.01$ ) decreased by 63.27% as compared to the G2 group. The level of serum proinflammatory cytokine (TNF- $\alpha$ ) was significantly decreased by 37.06%, 40.50%, 85.36% ( $p \leq 0.01$ ), 50.66% ( $p \leq 0.01$ ), 87.38% ( $p \leq 0.01$ ), and 58.63% ( $p \leq 0.01$ ) in the G4 (Cecal Slurry, LPS and *E. coli* along with untreated test formulation); G5 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation); G6 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15); G7 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation from day -15); G8 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation) groups, respectively as compared to the disease control (G2) group. On the other hand, the expression of TNF- $\alpha$  was reduced by 5.47%, 76.74%, 21.61%, 79.95%, and 34.27% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group (Figure 2). TNF- $\alpha$ , a pro-inflammatory cytokines play a wide role in the human body. These cell signaling protein (cytokine) significantly involved in systemic inflammation along with acute phase reaction. It mediates and regulates immune responses and inflammation. It also produce widespread deleterious effects when expressed in large amounts. It is produced in the heart by both cardiac myocytes and resident macrophages under conditions of cardiac stress, and responsible for various cardiac disease, elevated in congestive heart failure and potentiates heart failure [30]. TNF-alpha may also triggering and perpetuation of atherosclerosis. Treatment with biologic agents that inhibits TNF-alpha expression has various clinical benefits in inflammatory diseases such as rheumatoid arthritis (RA) and may be able to reduce cardiovascular risk [31]. Overall, in this experiment the Biofield Energy Treated test formulation and Biofield Energy Treatment *per se* reduced the level of TNF-alpha which might be helpful for the management of various inflammatory disorders.

#### Estimation of Serum IL-1 $\beta$

The effect of the test formulation and Biofield Energy Treatment *per se* was estimated using the level of serum IL-1 $\beta$ , and the results were graphically presented in the Figure 3. The disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na) + 0.5% CMC group (G2) showed value of IL-1 $\beta$  as  $90 \pm 7.2$  pg/mL, which was increased by 63.64% as compared with the normal control (G1,  $55 \pm 3.66$  pg/mL). Further, the positive control (Dexamethasone) treatment (G3) showed decreased serum IL-1 $\beta$  level by 15.87% i.e.,  $75.71 \pm 6.31$  pg/mL as compared to the G2 group. The level of IL-1 $\beta$  was decreased by 3.47%, 11.11%, 9.52%, and 6.35% in the G5 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation); G6 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15); G8 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation) groups, respectively, as compared to the disease control group (G2). Similarly, IL-1 $\beta$  level was decreased by 9.91%, 17.04%, 5.52%, 15.56%, and 12.59% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group (Figure 3). The experimental and clinical evidence reported that interleukin-1 beta (IL-1 $\beta$ ) plays both vascular and systemic contributor against conventional risk factors to atherosclerosis [32]. Another studies evidence in humans, suggests that IL-1 $\beta$  plays a role in insulin resistance, both T2DM and pre-diabetic states [33]. Therefore, in this experiment the Biofield Energy Treated test formulation and Biofield Energy Treatment *per se* reduced the level of IL-1 $\beta$ , which could be beneficial in the inflammatory disease conditions.

#### Estimation of Serum IL-6

The level of serum IL-6 was detected in all the experimental groups and was presented in Figure 4. The data suggested that disease control (Cecal Slurry, LPS and

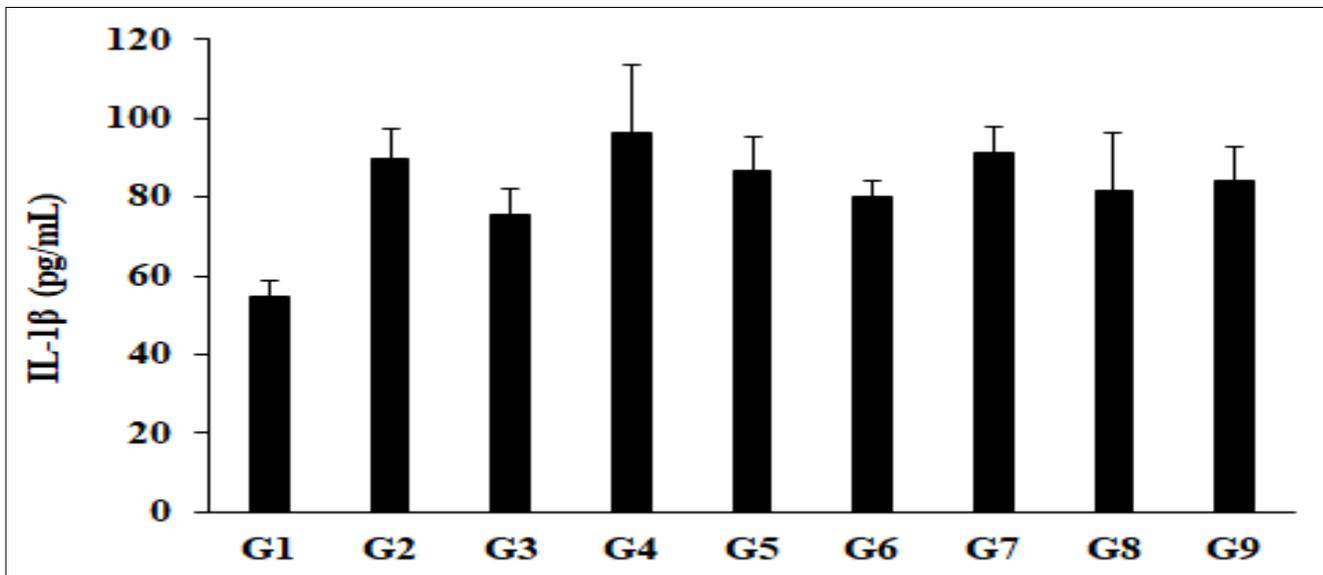


Figure 3. Expression the level of serum interleukin-1 $\beta$  (IL-1 $\beta$ ) after administration of Biofield Treated/Untreated proprietary test formulation and Biofield Energy Treatment *per se* to Sprague Dawley rats. G1 as normal control (vehicle, 0.5% w/v CMC-Na); G2 as disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na); G3 as reference item (Cecal Slurry, LPS and *E. coli* + Dexamethasone); G4 includes Cecal Slurry, LPS and *E. coli* along with untreated test formulation; G5 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation; G6 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15; G7 as Cecal Slurry, LPS and *E. coli* + Biofield Energy Treated test formulation from day -15; G8 group includes Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* + Biofield Energy Treated test formulation from day -15, and G9 group denoted Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* animals + untreated test formulation. Values are presented as mean  $\pm$  SEM (n=6-9).

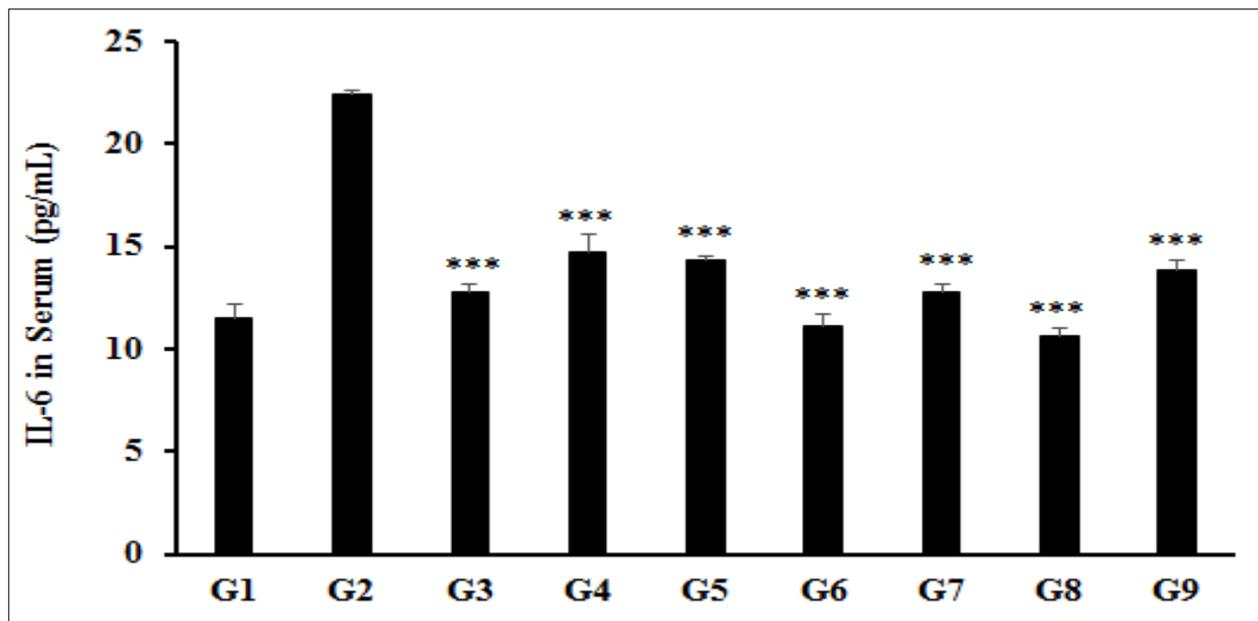


Figure 4. Expression the level of serum interleukin-6 (IL-6) after administration of Biofield Treated/ Untreated proprietary test formulation and Biofield Energy Treatment *per se* to Sprague Dawley rats. G1 as normal control (vehicle, 0.5% w/v CMC-Na); G2 as disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na); G3 as reference item (Cecal Slurry, LPS and *E. coli* + Dexamethasone); G4 includes Cecal Slurry, LPS and *E. coli* along with untreated test formulation; G5 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation; G6 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15; G7 as Cecal Slurry, LPS and *E. coli* + Biofield Energy Treated test formulation from day -15; G8 group includes Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* + Biofield Energy Treated test formulation from day -15, and G9 group denoted Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* animals + untreated test formulation. Values are presented as mean  $\pm$  SEM (n=6-9). \*\*\* $p \leq 0.001$  vs. Disease control group (G2).

*E. coli* + 0.5% CMC-Na) group (G2) showed value of IL-6 as  $22.44 \pm 0.21$  pg/mL, which was increased by 94.36% as compared with the normal control (G1,  $11.54 \pm 0.64$  pg/mL) group. While, the positive control (Dexamethasone) treatment (G3) significantly ( $p \leq 0.001$ ) decreased the level of IL-6 by 43.02% *i.e.*  $12.79 \pm 0.36$  pg/mL as compared to the G2 group. The level of interleukin-6 (IL-6) was significantly ( $p \leq 0.001$ ) decreased by 34.50%, 36.18%, 50.24%, 43.25%, 52.69%, and 38.23% in the G4 (Cecal Slurry, LPS and *E. coli* along with untreated test formulation); G5 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation); G6 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15); G7 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation from day -15); G8 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation) groups, respectively as compared to the disease control (G2) group. Moreover, the level of IL-6 was reduced by 2.58%, 24.04%, 13.36%, 27.78%, and 5.71% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group (Figure 4). There is increasing evidence that the metabolic syndrome is associated with a proinflammatory state. IL-6 has a dual effect; at some levels it acts as a defence mechanism but in chronic inflammation it is rather proinflammatory. Literature stated that IL-6 can be utilised as a treatment approach effectively for rheumatoid arthritis and other chronic inflammatory diseases [34]. Overall, here the Biofield Energy Treated test formulation and Biofield Energy Treatment *per se* reduced the level of IL-6, which could be beneficial in the inflammatory symptoms.

#### Estimation of Serum IL-10

The effect of the test formulation and Biofield Energy Treatment *per se* was estimated using the level of serum IL-10, and the results were graphically presented in the Figure 5. The disease control (Cecal Slurry, LPS and

*E. coli* + 0.5% CMC-Na) group (G2) showed value of IL-10 as  $8.71 \pm 1.86$  pg/mL, which was increased by 199.04% as compared with the normal control (G1,  $2.91 \pm 0.04$  pg/mL). Further, the positive control (Dexamethasone) treatment (G3) showed decreased serum IL-1 $\beta$  level by 86.54% *i.e.*,  $1.17 \pm 0.57$  pg/mL as compared to the G2 group. The level of IL-10 was decreased by 57.61%, 70.53%, 49.25%, 60.18%, 41.54%, and 58.89% in the G4 (Cecal Slurry, LPS and *E. coli* along with untreated test formulation); G5 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation); G6 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15); G7 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation from day -15); G8 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation) groups, respectively, as compared to the disease control group (G2). Similarly, IL-10 level was decreased by 30.43%, 19.80%, 6.01%, 38%, and 2.96% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group (Figure 5). The experimental and clinical evidence reported that interleukin-10 (IL-10) plays an important role in the control of inflammation [35]. Another study suggests that IL-10 can regulates the transcriptional modification in inflammation and autoimmune disease [36]. Therefore, in this experiment the Biofield Energy Treated test formulation and Biofield Energy Treatment *per se* reduced the level of IL-10, which could be beneficial in the inflammatory disease conditions.

#### Estimation of Serum Interleukin - 12

The effect of the test formulation and Biofield Energy Treatment *per se* on the level of serum interleukin -12, and the results were graphically presented in the Figure 6. The disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na) group (G2) showed value of IL-12 as  $9.51 \pm 0.80$  pg/mL, which was increased by 141.71% as

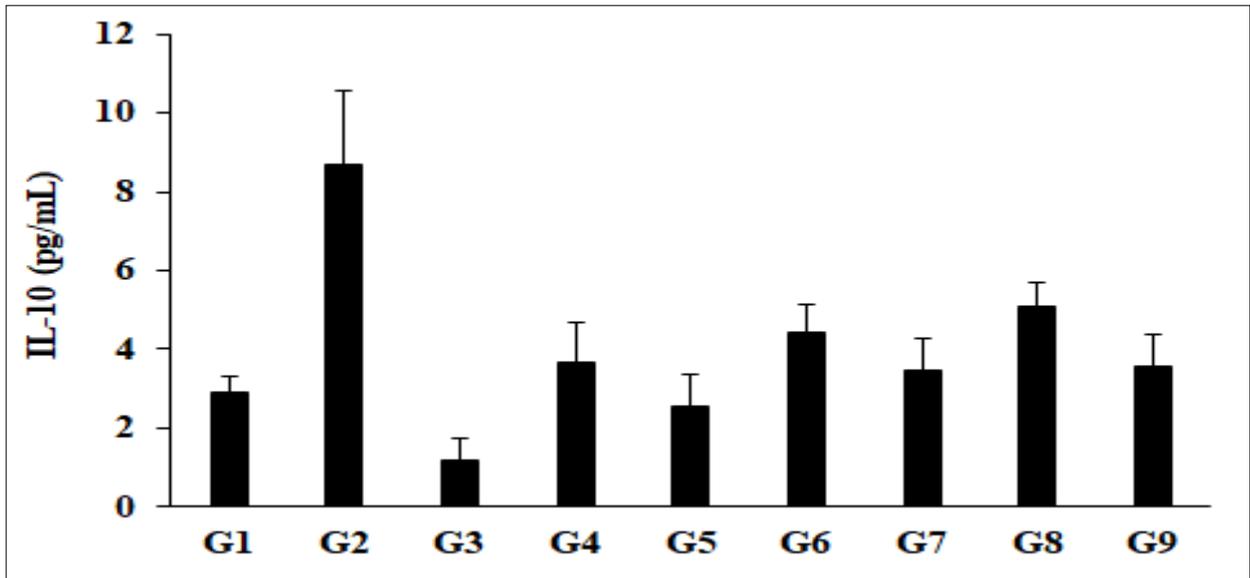


Figure 5. Expression the level of serum interleukin-10 (IL-10) after administration of Biofield Treated/ Untreated proprietary test formulation and Biofield Energy Treatment *per se* to Sprague Dawley rats. G1 as normal control (vehicle, 0.5% w/v CMC-Na); G2 as disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na); G3 as reference item (Cecal Slurry, LPS and *E. coli* + Dexamethasone); G4 includes Cecal Slurry, LPS and *E. coli* along with untreated test formulation; G5 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation; G6 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15; G7 as Cecal Slurry, LPS and *E. coli* + Biofield Energy Treated test formulation from day -15; G8 group includes Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* + Biofield Energy Treated test formulation from day -15, and G9 group denoted Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* animals + untreated test formulation. Values are presented as mean  $\pm$  SEM (n=6-9).

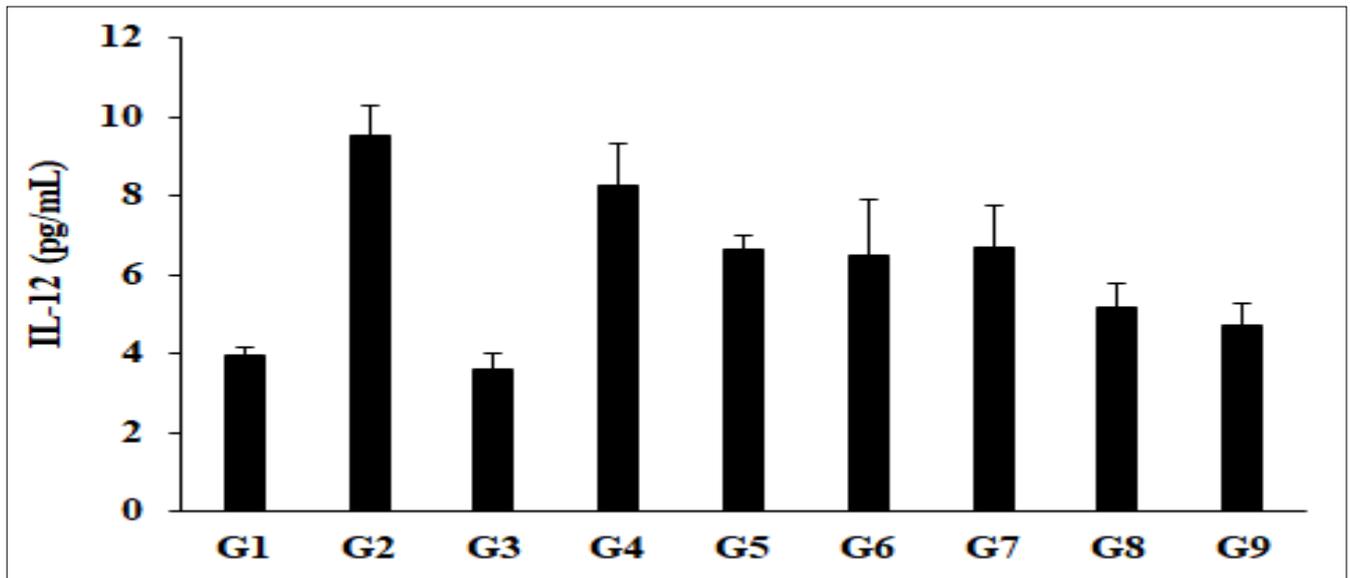


Figure 6. Expression the level of serum interleukin-12 (IL-12) after administration of Biofield Treated/Untreated proprietary test formulation and Biofield Energy Treatment *per se* to Sprague Dawley rats. G1 as normal control (vehicle, 0.5% w/v CMC-Na); G2 as disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na); G3 as reference item (Cecal Slurry, LPS and *E. coli* + Dexamethasone); G4 includes Cecal Slurry, LPS and *E. coli* along with untreated test formulation; G5 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation; G6 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15; G7 as Cecal Slurry, LPS and *E. coli* + Biofield Energy Treated test formulation from day -15; G8 group includes Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* + Biofield Energy Treated test formulation from day -15, and G9 group denoted Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* animals + untreated test formulation. Values are presented as mean  $\pm$  SEM (n=6-9).

compared with the normal control (G1,  $3.93 \pm 0.23$  pg/mL). Further, the positive control (Dexamethasone) treatment (G3) showed decreased serum IL-12 level by 62.37% i.e.,  $3.58 \pm 0.41$  pg/mL as compared to the G2 group. The level of IL-12 was decreased by 13.4%, 30.24%, 31.67%, 29.82%, 45.77%, and 50.54% in the G4 (Cecal Slurry, LPS and *E. coli* along with untreated test formulation); G5 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation); G6 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15); G7 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation from day -15); G8 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation) groups, respectively, as compared to the disease control group (G2). Similarly, IL-12 level was decreased by 19.49%, 21.13%, 19%, 37.42%, and 42.91% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group (Figure 6). Overall, in this experiment the Biofield Energy Treated test formulation and Biofield Energy Treatment *per se* significantly reduced the level of IL-12, which could be suppressed inflammatory conditions and simultaneously reduce the risks of inflammatory diseases.

#### Estimation of Serum IL-17

The level of serum IL-17 was detected in all the experimental groups and the data were presented in Figure 7. The disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na) group (G2) showed value of IL-17 as  $1546.74 \pm 249.27$  pg/mL, which was increased by 155.57% as compared with the normal control (G1,  $605.21 \pm 56.18$  pg/mL). Further, the positive control (Dexamethasone) treatment (G3) showed decreased serum IL-17 level by 60.37% i.e.,  $612.94 \pm 36.14$  pg/mL as compared to the G2 group. The level of IL-17 was decreased by 17.87%, 48.75%, 59.61%, 59.28%, 62.49%, and 58.65% in the G4 (Cecal Slurry, LPS and *E. coli* along

with untreated test formulation); G5 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation); G6 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15); G7 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation from day -15); G8 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation) groups, respectively, as compared to the disease control group (G2). Similarly, IL-17 level was decreased by 37.59%, 50.83%, 50.42%, 54.33%, and 49.66% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group (Figure 7). Interleukin-17 (IL-17) is a cytokine which elicits protection against extracellular bacterial and fungal infections and which plays important roles in inflammation [37]. Overall, here the Biofield Energy Treated test formulation and Biofield Energy Treatment *per se* reduced the level of IL-17, which could be beneficial in the inflammatory symptoms.

#### Estimation of Serum Interferon - $\gamma$

The level of serum interferon- $\gamma$  (IFN- $\gamma$ ) was detected in all the experimental groups and the data were presented in Figure 8. The disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na) group (G2) showed value of IFN- $\gamma$  as  $2.03 \pm 0.13$  pg/mL, which was increased by 317.88% as compared with the normal control (G1,  $0.49 \pm 0.08$  pg/mL). Further, the positive control (Dexamethasone) treatment (G3) showed decreased serum IFN- $\gamma$  level by 67.91% i.e.,  $0.65 \pm 0.18$  pg/mL as compared to the G2 group. The level of IFN- $\gamma$  was decreased by 2.05%, 49.56%, 24.09%, 23.7%, 56.98%, and 44.94% in the G4 (Cecal Slurry, LPS and *E. coli* along with untreated test formulation); G5 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation); G6 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15); G7 (Cecal Slurry, LPS and *E. coli*

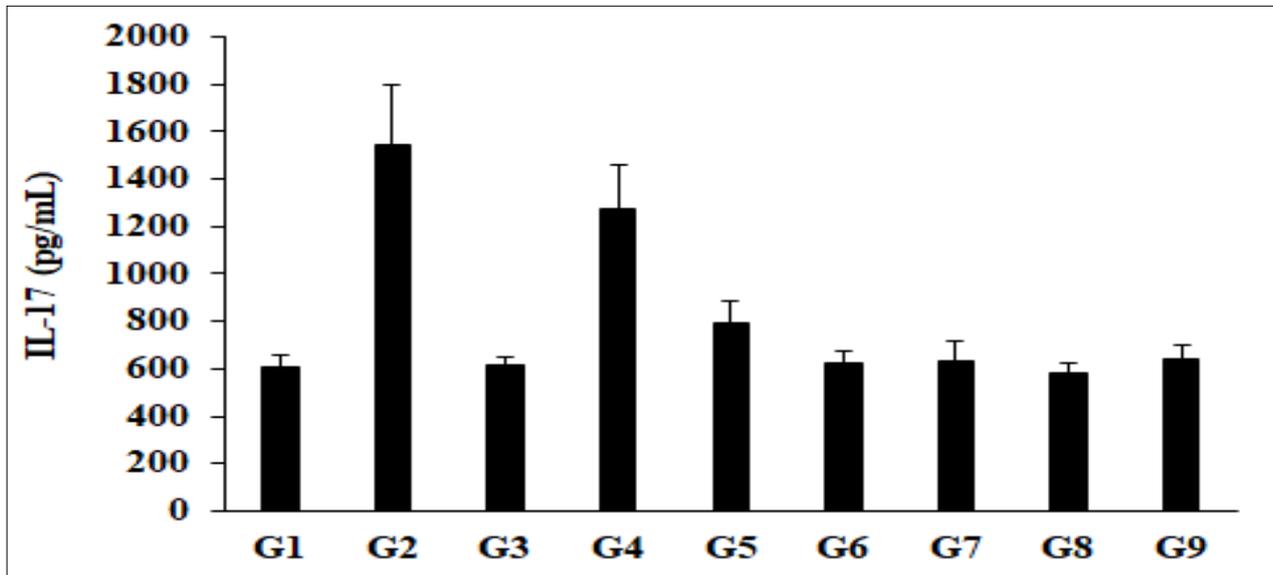


Figure 7. Expression the level of serum interleukin-17 (IL-17) after administration of Biofield Treated/ Untreated proprietary test formulation and Biofield Energy Treatment *per se* to Sprague Dawley rats. G1 as normal control (vehicle, 0.5% w/v CMC-Na); G2 as disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na); G3 as reference item (Cecal Slurry, LPS and *E. coli* + Dexamethasone); G4 includes Cecal Slurry, LPS and *E. coli* along with untreated test formulation; G5 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation; G6 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15; G7 as Cecal Slurry, LPS and *E. coli* + Biofield Energy Treated test formulation from day -15; G8 group includes Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* + Biofield Energy Treated test formulation from day -15, and G9 group denoted Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment *per se* animals plus the untreated test formulation. Values are presented as mean  $\pm$  SEM (n=6-9).

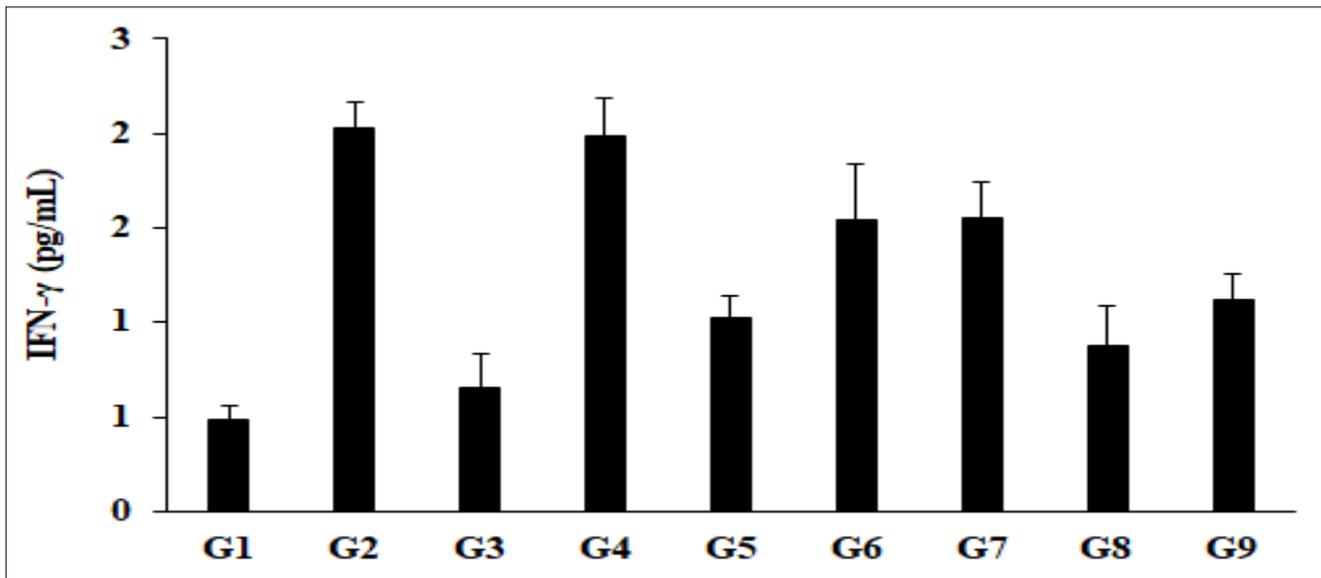


Figure 8. The effect of the test formulation on the level of serum interferon- $\gamma$  in Sprague Dawley rats. G1 as normal control (vehicle, 0.5% w/v CMC-Na); G2 as disease control (Cecal Slurry, LPS and *E. coli* + 0.5% CMC-Na); G3 as reference item (Cecal Slurry, LPS and *E. coli* + Dexamethasone); G4 includes Cecal Slurry, LPS and *E. coli* along with untreated test formulation; G5 as Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation; G6 group includes Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment per se to animals from day -15; G7 as Cecal Slurry, LPS and *E. coli* + Biofield Energy Treated test formulation from day -15; G8 group includes Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment per se + Biofield Energy Treated test formulation from day -15, and G9 group denoted Cecal Slurry, LPS and *E. coli* + Biofield Energy Treatment per se animals + untreated test formulation. Values are presented as mean  $\pm$  SEM (n=6-9).

along with the Biofield Energy Treated test formulation from day -15); G8 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation) groups, respectively, as compared to the disease control group (G2). Similarly, IFN- $\gamma$  level was decreased by 48.54%, 22.56%, 22.17%, 56.11%, and 43.84% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group (Figure 8). Interferon-gamma (IFN- $\gamma$ ) is a hallmark of innate and adaptive immunity. It also plays a vital role in host defense, its excessive release has been associated with the pathogenesis of chronic inflammatory and autoimmune diseases [38]. Overall, here the Biofield Energy Treated test formulation and Biofield Energy Treatment *per se* reduced the level of IFN- $\gamma$ , which could be beneficial for the treatment of various inflammatory disorders.

Experiment includes four preventive maintenance groups (G6, G7, G8 and G9). The findings showed the significant slowdown of inflammation-related symptoms and also reduced the chances of disease susceptibility. All-inclusive, it indicate that the Trivedi Effect<sup>®</sup> was found to be most effective and benefited to protect different kinds of diseases and also improve the overall health and quality of life.

## Conclusions

The level of cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-10, IL-12, IL-17, and IFN- $\gamma$  were estimated and compared with respect to the disease control and untreated test formulation groups. Serum TNF- $\alpha$  was decreased by 40.50%, 85.36%, 50.66%, 87.38%, and 58.63% in the G5 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation); G6 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* to animals from day -15); G7 (Cecal Slurry, LPS and *E. coli* along with the Biofield Energy Treated test formulation from day -15); G8 (Cecal Slurry,

LPS and *E. coli* along with Biofield Energy Treatment *per se* plus the Biofield Energy Treated test formulation from day -15), and G9 (Cecal Slurry, LPS and *E. coli* along with Biofield Energy Treatment *per se* animals plus the untreated test formulation) groups, respectively as compared to the disease control (G2) group. IL-1 $\beta$  was decreased by 17.04%, 15.56%, and 12.59% in the G6, G8, and G9 groups, respectively as compared to the untreated test formulation (G4) group. Moreover, the level of serum IL-6 was significantly reduced by 36.18%, 50.24%, 43.25%, 52.69%, and 38.23% in the G5, G6, G7, G8, and G9 groups, groups, respectively, as compared to the disease control group (G2). Additionally, IL-10 was decreased by 70.53%, 49.25%, 60.18%, 41.54%, and 58.89% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the G2 group. Further, IL-12 was decreased by 30.24%, 31.67%, 29.82%, 45.77%, and 50.54% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the G2 group. IL-17 was reduced by 48.75%, 59.61%, 59.28%, 62.49%, and 58.65% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the G2 group. Besides, IFN- $\gamma$  level was reduced by 49.56%, 24.09%, 23.7%, 56.98%, and 44.94% in the G5, G6, G7, G8, and G9 groups, respectively as compared to the G2 group. Altogether, the Biofield Energy Treated test formulation and Biofield Energy Healing Treatment (the Trivedi Effect<sup>®</sup>) *per se* showed fruitful results with respect to different inflammatory biomarkers (cytokines) in the preventive maintenance group, G6 as well as other preventive maintenance groups (G7, G8, and G9) in Cecal Slurry, LPS and *E. coli* induced systemic inflammatory response syndrome model rat model study. It also helped to slowdown the inflammatory disease progression and disease-related complications. The study data showed that Biofield Energy Treated Test formulation and Biofield Energy Treatment *per se* would be one of the best treatment strategies to prevent the manifestation of diseases. Thus, the Biofield Energy Treatment might act as a preventive maintenance therapy to maintain and improve the overall health and quality of life and simultaneously reduce the severity of acute/chronic

diseases. The test formulation can also be used against rheumatoid arthritis (RA), fibromyalgia, aplastic anaemia, Addison disease (AD), multiple sclerosis, myasthenia gravis, psoriasis, Crohn's disease, ulcerative colitis, dermatitis, hepatitis, Parkinson's, stroke, etc.

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