Modulatory Effect of Ginger Extract on Albino Rats Induced by D-Galactosamine and lipopolysaccharide

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Received: 20 November 2016 / Accepted: 22 December 2016 / Publication date: 05 January 2017

ABSTRACT

The present study describes the participation of (LPS) and (DGa1N) in septicemia and points to Ginger as a critical medicinal plant of resistance to this injury. Septic shock, in which severe sepsis and multiple organ dysfunction syndromes represent different stages of a pathophysiological process, organ failure, and eventually result in death. This complication results from a response to activation of the pro-inflammatory and anti-inflammatory cytokine cascades. Kupffer cells, resident macrophages of the liver, activated with lipopolysaccharide (LPS) release pro-inflammatory cytokine. D-Galactosamine (DGa1N), a hepatocyte-specific inhibitor of RNA synthesis, is known to sensitize animals to the lethal effects of LPS. In the present study, we seek to reverse some altered parameters, Physiological, immunological and histopathological, to normal values of rats treated with ginger. Septicemia was induced in male albino rats by the intraperitoneal induction of (583.3 mg) DGa1N and (0.233 mg) LPS/kg body weight. Expression levels of TNF-α, IL-6, IL-4 and IL-10 were detected by RT-PCR for mRNA of liver, spleen, and thymus. Lipid peroxidation and glutathione peroxidase levels were carried out spectero-photometrically. Histopathology, liver, kidney and spleen sections were stained with hematoxylin and eosin. The data showed treatment with ginger extract of injured rats induced significant ameliorative effect in Lipid peroxidation levels, glutathione peroxidase and expression of TNF-α level and IL-4, IL6 and IL-10 levels.

Key words: Lipopolysaccharide; D-galactosamine; Zingiber officinale; cytokines

Introduction

Lipopolysaccharide (LPS), a component of the cell wall of Gram-negative bacteria, is also the ligand of Toll-like receptor 4 (TLR4) and often elicits an uncontrolled inflammatory response, organ failure, and even death (Savva and Roger, 2013; Hartmann et al., 2015). LPS stimulates monocytes/macrophages via TLR4, which belongs to the TLR family (Akira et al., 2006). LPS is recognized by TLR4 together with accessory molecules such as myeloid differentiation protein-2 and cluster of differentiation 14 (CD14), and TLR4 transduces LPS signaling via both myeloid differentiation factor 88 (MyD88)-dependent and MyD88- independent pathways, each of which activates nuclear factor-kβ (NF-kβ) (Kobayashi et al., 2006).

D-galactosamine (DGa1N) is a well-known chemical substance for inducing manifestation of experimental hepatitis; in addition to its properties as a transcriptional inhibitor, thus DGa1N is connected with an insufficiency of UDP-glucose and UDP-galactose and the loss of intracellular calcium homeostasis; these changes affect cell membranes and organelles and the synthesis of proteins and nucleic acids (Ferenčíková et al., 2003). Lipopolysaccharide/D-galactosamine (LPS/DGa1N) treated mice are a known model of acute liver injury. DGa1N greatly increases the sensitivity of mice to LPS-induced hepatotoxicity) Shang et al., 2009 ; Wang et al., 2013). DGa1N is very toxic to the liver which causes liver injury resembling viral hepatitis with inflammation, degeneration and necrosis. DGa1N alters liver functions through depletion of uridine pools and so limiting synthesis of RNA and protein (Jung et al., 2013).

Administration of DGa1N and LPS lead to an excessive generation of reactive oxygen species (ROS) which through their oxidative damage lead to acute hepatitis (Moore et al., 2001 ; Sheik and Thiruvengadam, 2013). Activation of TLR4 in response to LPS cause production of ROS and increased pro-inflammatory cytokines expression such as tumor necrosis factor-α (TNF-α),
interleukin-6 (IL-6), interleukin-12 (IL-12) and therefore increased ROS production (Sheik and Thiruvenkadam, 2013). Interleukin-4 (IL-4) and interleukin-10 (IL-10) are key anti-inflammatory factor and pleiotropic cytokine produced by a variety of cell types among which monocytes/macrophages are the main sources (Zhu et al., 2012).

Ginger (Zingiber officinale), has been used as a refrigerant, astringent and flavoring agent, and as a digestive in medicine. Its rhizomes paste has been traditionally applied for improving the healing of wounds, cuts, and antipruritic. Its broad spectrum of biological activities includes antioxidant, antimicrobial, antitumor or anti-diabetic effects (Srivastava et al., 2006). More recently, it has been shown that ginger and some of its constituents are effective against cytokines synthesized and secreted at sites of inflammation (Grzanna et al., 2005). This species contains biological active constituents including terpenes and oleoresin. From terpene, the major identified components are sesquiterpene hydrocarbons and phenolic compounds such as gingerol and shogaol. Gingerols known as phenolic ketones, can be converted to shogaols, zingerone, and paradol which produce the hot sensation in the mouth (Rahmani et al., 2014).

Masuda (2004) identified more than 50 compounds including gingerols or diaryl-heptanoids obtained from ginger with antioxidant activity. The ginger causes the suppression of both cyclooxygenase and lipoxygenase metabolites and arachidonic acid (Dugasani et al., 2010). According to Li (2011) shogaol and (6)-dehydroshogaol has been able to inhibit Nitric oxide production in LPS stimulated macrophages. Because of the low toxicity of ginger and the broad spectrum of its biological and pharmacological applications, it has been increasingly used (Aly et al., 2013).

This study aimed to investigate the ameliorative effect of ginger extract against oxidative stress and inflammation induced by LPS/DGa1N.

Materials and Methods

Animals:

Thirty adult male albino rats weighing (100-120 g.) were housed in a well-ventilated room for two weeks before carrying out the experiment, feeding on commercial rodent food pellets and water.

Chemicals:

Lipopolysaccharide (LPS) was extracted from (E.coli O127:B8) and D-galactoseamine hydrochloride (DGa1N) were obtained from Sigma-Aldrich chemical St. Louis, MO, USA. Lipid peroxidase and glutathione peroxidase kits were obtained from Bio-diagnostics Cairo, Egypt. Molecular kits were obtained from Thermo-scientific Cairo, Egypt. All other chemicals were obtained commercially as reagent-grade products.

Experimental design:

All animals were divided into two groups. The control group (GI) consists of 5 rats were left for two weeks to start at the same date as treated groups, then, administered intra-peritoneal (i.p) with Phosphate buffer saline (PBS). Ginger group (GII) consists of 25 rats were pretreated orally with ginger extract (200mg/kg) (Bhandari et al., 2003), for two weeks before induction with LPS/DGa1N(0.233 mg/kg, 583.3 mg /kg, respectively) intra-peritoneal (Hussein et al., 2011). Twenty rats in group II were sacrificed after 6, 12, 24 and 48 hours of induction by LPS/DGa1N (five rats per each hour). The last five rats were post-treated with ginger for another two weeks then sacrificed. The animals were sacrificed by cervical decapitation, blood samples were immediately collected. After animal dissection, liver, kidney, spleen and thymus were collected for histological and molecular studies.
Measurements of lipid peroxide:

Lipid peroxide level was determined in serum according to method described by Ohkawa (1979).

Measurements of glutathione peroxidase level:

Glutathione peroxidase level was determined spectrophotometrically according to the method described by Weinhold (1991).

Interleukins measurements with the use of reverse transcription polymerase chain reaction method (RT-PCR):

Liver, spleen and thymus samples were obtained to be used for total RNA isolation according to the manufacturer’s instructions of thermo scientific Laboratories. mRNA was purified then; the reverse transcription from mRNA to cDNA was processed by Maxima® first strand cDNA synthesis kit for RT-PCR.

Expressions of selected genes were evaluated using RT-PCR of cDNA originating from total RNA, with the help of DreamTaq Green DNA Polymerase master mix. PCR amplification was performed with a thermal cycler for 30 cycles (30 seconds denaturation at 95°C, 30 seconds annealing at 50°C, and 5 minute elongation at 72°C). A 10 ml portion of each PCR product was electrophoresed on a 2% agarose gel and visualized by ethidium bromide staining.

(Oligonucleotide primers)

<table>
<thead>
<tr>
<th>Serial number</th>
<th>Name</th>
<th>Sequence</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>TNF-forward</td>
<td>5'-ATCCGAGATGTGGAACTG-3</td>
</tr>
<tr>
<td>2</td>
<td>TNF-reverse</td>
<td>5'-CACGTAGTCGGGGCAGCC-3</td>
</tr>
<tr>
<td>3</td>
<td>IL-10-forward</td>
<td>5'-TGTGGCTGCTTTACTG-3</td>
</tr>
<tr>
<td>4</td>
<td>IL-10-reverse</td>
<td>5'-GCAGTTGATGAAGATGTC-3</td>
</tr>
<tr>
<td>5</td>
<td>IL-4—forward</td>
<td>5'-CCCCACCTTGCCTGCACC-3</td>
</tr>
<tr>
<td>6</td>
<td>IL-4—reverse</td>
<td>5'-TGAGTTTGACCGCTGAC-3</td>
</tr>
<tr>
<td>7</td>
<td>IL-6—forward</td>
<td>5'-CCTCTTGGGACTTGAT-3</td>
</tr>
<tr>
<td>8</td>
<td>IL-6—reverse</td>
<td>5'-GTAAGTTGTTCCTCACA-3</td>
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Histological Studies:

Liver, kidney, and spleen samples were dissected and fixed in 10% formal saline, embedded in paraffin, and cut into 5 µm thickness in microtome; then stained with hematoxylin and eosin.

Statistical analysis

The data of all groups were represented as means ± Standard Error (SE) and were statistically analyzed using the T test, one way analysis of variance (ANOVA test using the SPSS program version 16.0) to analyze specific difference between means .

Results

Serum lipid peroxide levels were demonstrated in (Fig.1), where the control group (9.18±0.34 nmol MDA/ml), the group II Which pretreated with ginger extract before LPS/DGa1N induction at 6, 12, 24, 48 hours was increased to be higher than control group after 6 hours (19.73±0.51 nmol MDA/ml), 12 hours (15.9±0.33nmol MDA/ml), 24 hours (20.31±0.67 nmol MDA/ml), 48 hours (20.99±0.32nmol MDA/ml). In contrast, the rats which post-treated with ginger extract for two weeks after LPS/DGa1N induction (14.94±1.61 nmol MDA/ml) is higher than control, but lower than 6, 12,
24 and 48 hours groups. This results showed a high significant difference of lipid peroxide level between all groups (P<0.001).

Nevertheless, the Glutathione peroxidase (GPx) level of normal control group (2.53±0.24U/g.Hb). However, its level in the Group II after 6,12,24,48 hours decreased comprised with control, 6 hours (1.01±0.04U/g.Hb), and after 12 hours (1.25±0.08U/g.Hb), 24 hours (0.99±0.04 U/g.Hb) and (0.82±0.03U/g.Hb), while after Two weeks of post treatment with Ginger extract the level of glutathione peroxidase (Gpx) (1.85±0.12U/g.Hb) which was lower than control but higher than pretreated groups 6,12,24 and 48 hours. This results showed a high significant difference of lipid peroxide level between all groups (P<0.001). (Fig 2.)

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**Fig.1:** Histogram Showing lipid per oxide level (nmol MDA/ml) in serum of Group I (normal control) and Group II treated with ginger (6, 12, 24, 48 hours, and Two weeks).

***:- significant difference at p value <0.001

**Fig.2:** Histogram Showing Glutathione peroxidase level (U/g.Hb)) in Group I (normal control) and Group II treated with ginger (6,12,24,48 hours, and Two weeks).

***:- significant difference at p value <0.001
Expression of Pro-inflammatory cytokines (TNF-α) and (IL-6):

Tumor necrosis factor-α (TNF-α).

Results of PCR (Fig.3) showed that TNF-α expression in liver, spleen and thymus of group II which pretreated with ginger after 6, 12, 24 and 48 hours of LPS/DGa1N induction was higher than control. On the other hand post treatment with ginger extract for another two weeks after LPS/DGa1N showed a modulation of TNF-α expression.

Interleukin-6 (IL-6).

Results of PCR (Fig.4) showed that IL-6 expression in liver of groups pretreated with ginger before LPS/DGa1N after 6, 12, and 48 hours Lower than control, but after 48 hours was higher than control. On the other hand post treatment with ginger for two weeks after LPS/DGa1N showed expression lower than control (Fig.4 a). In the spleen, expression of IL-6 increased by the time of stimulation until 48 hours of stimulation in comparison with control. Post treatment with ginger leads to decrease in the rate of expression to reach near that expressed in control rats (Fig.4 b). The expression of IL-6 in thymus showed nearly the same expression rate in the liver (Fig.4 c).

Expression of anti-inflammatory cytokines (IL-4, IL-10)

Interleukin-4 (IL-4)

Results of PCR in Fig. (5) showed that IL-4 expression in liver of groups pretreated with ginger before LPS/DGa1N after 6, 12, 24 and 48 hours higher than control. On the other hand post treatment for another two weeks after LPS/DGa1N showed expression higher than control but lower than the 6,12,24,48 hours respectively (Fig 5 a).
Fig. 4: IL-6 expression in Group I (normal control) and Group II at (6, 12, 24, 48 hours, and Two weeks). (a) IL-6 expression in liver which show high expression at 24 hours ,while it the same of control at 12,48hour, Two weeks, and less than control at 6 hours . (b) IL-6 expressions in spleen which show high expression at 6, 12, 24, 48 hours, while it moderate at Two weeks comparing with control. (c) IL-6 expression in thymus that show slightly risen in expression of IL-6 at 6, 24,48hours and it show the same expression of control at 12hours and Two weeks.

Fig. 5: IL-4 expression in in Group I (normal control) and Group II at (6, 12, 24, 48 hours, and Two weeks). (a) IL-4 expression in liver which shows lightly highness expression at 6,24,48 hours ,while it moderate at 12hour,and it is normal at Two weeks comparing with control. (b) IL-4 expression in spleen which show slightly risen expression at 24,48 hours, while it seems normal at 6,12,48 hours and Two weeks comparing with control. (c) IL-4 expression in thymus that show the same expression of control at 6, 24,48hours, while it showed little expression at 48hours and Two weeks comparing with control.
In spleen, IL-4 expression increased until the first 24 hours after stimulation and then decreased in comparison with other hours but still higher than control (Fig. 5 b). After two weeks of treatment with ginger the expression decreased to be somewhere the same of control. The expression in thymus was increased after 6 hours and then decreased sharply after 24 hours of stimulation. By 24 hours of stimulation the expression was so high in comparison with control and slightly decreased by time. Post treatment with ginger leads to a sharp decrease in IL-4 expression in thymus (Fig. 5 c).

**Interleukin-10 (IL-10).**

Results of PCR (Fig. 6) showed that IL-10 expression in liver of groups pre-treated with ginger before LPS/DGa1N after 6, 12, 24, and 48 hours higher than control. On the other hand the ginger treated group for another two weeks after LPS/DGa1N showed expression nearly same the control but lower than the 6, 12, 24, 48 hours. In spleen increased after 6 hours of stimulation and then decreased by 12 hours. The expression rate reaches its peak after 24 hours of stimulation (Fig. 6 b). Thymus IL-10 expression increased by time of stimulation until 24 hours then decreased by 48 hours (Fig. 6 c). Post treatment with ginger showed a remarkable adjustment of IL-10 expression in liver, spleen and thymus (Fig. 6).

![IL-10 expression in liver, spleen and thymus](image)

**Fig. 6:** IL-10 expression in Group I (normal control) and Group II at (6, 12, 24, 48 hours, and Two weeks). (a) IL-10 expression in liver which show moderate expression at 12, 24, 48 hours, while it the same of control at 6 hours, Two weeks. (b) IL-6 expressions in spleen which show high expression at 6, 24 hours, while it moderate at 48 hours comparing with control, and show nearly the same expression of control at 12 hours and Two weeks. (c) IL-6 expression in thymus that show nearly the same expression of IL-6 of control at 12, 24, 48 hours and it show expression less than control at 6 hours and Two weeks.

**Histological studies**

Histopathological examination of liver sections from control group revealed normal architecture, (Fig. 7) Pretreated groups after 6, 12, 24, 48 hours liver sections showed loss of architecture, prominent inflammatory collections, pyknosis and vacuolation in a great manner. On the other hand, the ginger post-treated group for two weeks after LPS/DGa1N induction showed a degree of improvement in comparison with 6, 12, 24 and 48 hours, but still showed some degeneration.
Fig. 7: Light photomicrographs of rat liver (H&E stains, Magnification 50 μm equivalent 400x): (A) Control rat liver section showing normal central vein (CV) and hepatocytes (h). (B), (C), (D), (E) Pre-treated groups by ginger at 6, 12, 24 and 48 hours showed dilated central vein, great number of pyknotic nuclei (thick black arrow and vacuolation (f) post treated group for two weeks after LPS/DGa1N showed some congestion and pyknotic nuclei. (Thick black arrows refer to pyknosis, thin black arrows refer to vacuolation, thick red arrows refer to congestion, thin red arrows refer to necrosis)
Fig. 8: Light photomicrographs of rat liver (H&E stains, Magnification 50 µm equivalent 400x) : (A) Control rat kidney section showing normal renal glomeruli (G) and the proximal tubules (p) are lined with typical thick cubic epithelium and distal (d) convoluted tubules are lined with the relatively low simple cubic epithelium. Organization of the glomeruli and a flat epithelium lining the Bowman's capsule with distinct bowman's space (bs) can be seen.(B),(C),(D),(E) Pre-treated groups by ginger at 6,12,24 and 48 hours showing severe degeneration in glomeruli which appeared congested , proximal(P) and distal(d) tubules showed excessive cast formation ,epithelial cells show exfoliation, vacuolation was detected also ,sever extravasation was shown).(F)Post treated group with ginger which show severe degeneration, wide bowman's space , proximal(P) and distal(d) tubules which showed loss of architecture, and vacuolation ,exfoliated epithelial cells.(Thick black arrows refer to exfoliated cells ,thin black arrows refer to vacuolation, thick red arrows refer to congestion ,thin red arrows refer to cast formation ,thick blue arrows refer to macrophages ,thin blue arrows refer to extravasation)
Fig. 9: Light photomicrographs of rat liver (H&E stains, Magnification 50 µm equivalent 400x) : (A) a spleen section at white pulp of a normal control rat, showing scattered macrophages (Ma), and megakaryocyte (Me) precursor of platelets, Erythrocytes(E) could be detected also. Blood sinus (Bs). (B),(C),(D),(E) Pre-treated groups by ginger at 6,12,24 and 48 hours showing excessive hemosiderin granules (Thick black arrow) and highly, congestion, beside dilated sinus (Bs). (F) Post treated group with ginger which showing diffused hemosiderin granules and congestion. (Thick black arrows refer to hemosiderin granules, thin black arrows refer to congestion)

On the other hand examination of kidney sections of control group showed cortex of the kidney distinguished by distal, proximal tubules and characteristic renal corpuscles . Each renal corpuscle
consists of an outer envelope of simple squamous epithelium (Bowman's capsule) surrounding a fluid-filled space (Bowman's space) within which is suspended a glomerulus (G). While pretreated groups after 6, 12, 24, 48 hours kidney sections showed severe degeneration of proximal tubules, besides high vacuolation, and showed cast formation at lumen of tubules. Exfoliation of tubule’s epithelial cells was detected, the Bowman's space became wider, and the glomeruli were seen congested and vacuolation was detected. The post treatment with ginger for two weeks didn’t show an improvement in kidney sections. In contrast spleen sections of normal control showed the basic structure of parenchyma (white and red pulp). Blood vessels enter and leave the parenchyma via septa. The white pulp contains the lymphocytes of the spleen (Fig 9). The pretreated group by ginger after 6, 24, 48, and two weeks showed remarkable congestion and hemosiderin granules appeared, while post treatment spleen sections showed some improvement in tissue as congestion was less than pretreated groups.

Discussion

Many approaches to suppress the effects of inflammatory mediators have been unsatisfactory for effective treatment of Gram-negative bacteria (Bochud et al., 2003). This prompted us to use a medicinal plant, Ginger, to treat bacterial infection causing liver injury.

This work describes participation of DGa1N and LPS in septicemia and points to Ginger as a critical medicinal plant of resistance to this injury. Histological disorder is accompanied by the level of some cytokines, such as pro-inflammatory TNF-α and IL-6 and anti-inflammatory IL-4 and IL-10. On the other hand, the oxidative stress play great role in multi-organ failure. Lipid peroxide and glutathione peroxidase have the major role in oxidative stress.

Kupffer cells are reported to be the key components of the innate immune system of the liver in response to LPS. It has been reported that LPS-stimulated Kupffer cells secrete higher levels of the immunosuppressive cytokine IL-10, which in turn leads to inactivation of Natural Killer (NK) cell function (Krueger et al., 2011).

Stimulation of the liver spleen and thymus by LPS, the immune components part of these organs secrete a pro-inflammatory cytokines such as interleukin-1 (IL-1), tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), monocyte chemo attractant protein-1 (MCP-1) and other many pro-inflammatory mediators (Wang et al., 2016).

The effect of LPS is transduced throughout toll like receptor-4 (TLR-4) (Park and Lee, 2013). TLR-4 then induces signals those stimulates the expression of NF-kB proteases which leads to expression of reactive oxygen and nitrogen species (Wittebole et al., 2010). These mediators and pro-inflammatory cytokines stated to trigger the organ cells death (Schmöcker et al., 2007).

Filtration of different types of leukocytes into the infected organ was reported to be due to chemo-attractant in a gradient manner (Antoniades et al., 2008). Monocytes were reported to be chemo-attracted to liver and spleen from the bone marrow through the activation of bone marrow by LPS (Serbina et al., 2008; Karlmark et al., 2009). Induction of a large dose of this agent into rats induces a hepatic necrosis resembling the effects of human viral hepatitis, and nuclear fragmentation is an early event after induction of DGa1N (Shinozuka et al., 1973; Funayama et al., 2001).

Results of present study revealed a significant elevation in Lipid peroxidation level after induction of LPS/DGa1N in all groups, according to Jiang (Jiang et al., 2005). This may be due to excessive production of ROS resulted from sepsis, which responsible for the free radicals mediated cellular injury which was confirmed by histopathological experiments.

A significant low level of glutathione peroxidase was observed in this study after induction by LPS/DGa1N may be due to elevation in the rate of lipid peroxidation that produces high amount of lipid peroxides causing oxidative damage of tissues and inactivation of glutathione peroxidase (GPx), which are associated with high amount with hydrogen peroxide H2O2 that damages the membrane and biological structure of tissues (Santhakumari et al., 2003).

The present study revealed that lipid peroxidase level decreased and GPX level increased in groups post-treated with ginger extract for two weeks, this may due to antioxidant properties of ginger which suppress the lipid peroxidation (Chilakala et al., 2015).

Endotoxemia -induced toxicity is characterized by disturbed intracellular Redox balance and excessive reactive oxygen species (ROS) accumulation Leading to DNA proteins and membrane lipid
damages. Increased ROS production was responsible for the changes in gene expression (Kong and Lin, 2010).

In present study we noticed that examined pro-inflammatory cytokines (TNF-α and IL-6) showed an increase of expression in both liver and spleen by time of induction. Although, TNF-α is secreted by T-cells (Sun and Shang, 2015), the expression in thymus was so low but also increased by time of induction. The expression in liver and spleen was high in compassion with control and reach its maximum after 12hours of induction in liver and 24h in spleen. This may be due to the high spleen T-cell content and therefore cytokine tolerance was somewhat long (until 24hours) in case of liver it goes with the normal fluctuation of pro-inflammatory cytokines expression (An 2009; Fridlender and Albelda 2012). in case of IL-6, it showed a frame of expression near to that of TNF with respect to the normal expression rate in pro-inflammatory models that found in all examined tissues (liver, spleen and thymus)(An 2009 ). IL-6 showed a very high expression in liver as the IL-6 from those early produced pro-inflammatory cytokines as liver cells kupffer cells make the main innate immune component of the liver (Wang et al., 2016) Regarding both TNF-α and IL-6 as a whole the expression was increased by infection to mediate the signals for the nucleus of the cell in different ways of mechanisms (Tjardes et al., 2002 ; Han and Ulevitch, 2005).After two weeks of treatment with ginger extract the expression rate of cytokines was near to that of control and this recommend the modulatory effect of ginger in control of the early inflammatory process throughout the control of the cytokine secreted (Grzanna et al., 2005).

In case of anti-inflammatory cytokines (IL-4 and IL-10) we noticed that the expression rate was low in comparison by control and increased again by time until 24h after induction and this can explain the decline rate followed by the pro-inflammatory ones. This is because Septicemia and oxidative stress exhibited activation of NF-kβ which binds to nuclear DNA and modulates the expression of TNF-α (Oeckinghaus and Ghosh, 2009).

The histological injuries such as inflammation induced by D-GalN/LPS were markedly improved by ginger, which showed a modulatory effect on liver, spleen tissues. The results showed that ginger was scavenging free radical by its potent antioxidant. These results were cleared by the data in which ginger reduced the level of serum malondialdehyde acting as lipid peroxidation marker and increased the serum level of antioxidant enzyme. (Siddaraju and Dharmesh, 2007). Unlike liver and spleen, the improvement in kidney tissues wasn't clear.

In conclusion, the present data demonstrates that pre and post-treatment with ginger extract has a protective effect in restoring the balance between pro and anti-inflammatory cytokines expression levels, reducing lipid peroxidation and increasing glutathione peroxidase effect. Thus ginger extract may be efficient for amelioration the toxicity caused by LPS/DGa1N.

References


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