Effect of Dietary Ginger as Feed Additive on Gastrointestinal Integrity, Hepatic Condition and Metabolic Parameters of Female Mice

Aliaa A. Ismail¹, Dalia W. Zeidan², Amani A. Almallah³, Aya A. Gaber⁴ and Heba M. A. Abdelrazek⁵*

¹Department of Pathology, Faculty of Veterinary Medicine, Suez Canal University, Ismailia, Egypt.
²Department of Home and Economics, Nutrition and Food Science Branch, Faculty of Education, Suez Canal University, Ismailia, Egypt.
³Anatomy and Embryology Department, Faculty of Medicine, Suez Canal University, Egypt.
⁴Postgraduate at Department Pharmacology Department, Faculty of Veterinary Medicine, Suez Canal University, Ismailia, Egypt.
⁵Department of Physiology, Faculty of Veterinary Medicine, Suez Canal University, Ismailia, Egypt.
*Corresponding Author E-mail: hebaabdelrazekvet@gmail.com

https://dx.doi.org/10.13005/bpj/2113

(Received: 11 January 2021; accepted: 04 March 2021)

Present work aimed to study the influence of dietary ginger inclusion in female mice on gastrointestinal integrity, hepatic condition and metabolic parameters. Thirty female mice (18± 2 g) were assigned into 3 groups; control group fed standard rodents’ basal diet, ginger 2% and ginger 5% mice were basal diet supplemented with 2% and 5% ginger powder, respectively for 30 days. Weight gain, feed conversion (FCR) and efficiency (FER) ratios were recorded. Serum liver enzymes, lipid profile, total protein and albumin were measured beside estimation of hepatic reduced glutathione (GSH) and malondialdehyde (MDA). Gastric, intestinal and hepatic histopathology were performed as well as intestinal histomorphometry. Results revealed improvement in FCR, FER and most tested biochemical parameters, in 2% ginger group than control. Hepatic MDA and GSH were significantly (P<0.05) increased and decreased, respectively in 2% ginger group. However, ginger 5% group exhibited improvement in intestinal histomorphometry while adversely affected gastric mucosa and hepatic tissue histopathology. Also increased hepatic MDA and reduced GSH were prominent in 5% ginger group along with mild gastric and hepatic lesions. The administration of dietary ginger by 2% dose could be beneficial to mice model however, increasing the dose to 5% could produce adverse effects on hepatic integrity and gastric mucosa.

Keywords: Dietary, Ginger, Liver, Intestinal histomorphometry.

The use of feed additives, in livestock production (Singh, 2016) as well as human feed (Wang and Shelomi, 2017) is gaining special interest owing to many reasons. Feed additives can improve digestibility and have antimicrobial, anti-inflammatory, antioxidant and immune-stimulant activities. Moreover, the ban on use of certain antibiotics due to harmful residual effects on human health and development of microbial resistance to antibiotic drugs (Sarker et al., 2010). Herbal feed additives play a significant role in health and nutrition. Several feed additives like prebiotics, probiotics, plant extracts and organic acids had...
been demonstrated to have beneficial influences on animal production (Kumar et al., 2014).

Ginger (Zingiber officinale) is one of the most well-known, safe medicinal plants with only few and insignificant adverse effects, that belongs to the Family Zingiberaceae (Mekuriya and Mekibib, 2018). Ginger is also worldwide used as cooking spice, flavoring agent and food preservation (Ajayi et al., 2013). In traditional medicine, ginger was used as a carminative or anti-flatulent. More than 60 different bioactive constituents are present in ginger, which have been allocated into volatile and nonvolatile compounds (Ahmad et al., 2015). The powdered rhizome contains 3-6% fatty oil, 9% protein, 60-70% carbohydrates, 3-8% crude fiber, about 8% ash, 9-12% water and 2-3% volatile oil (Zadeh and Kor, 2014). Ginger has prominent medicinal characteristics such as its pungent and stimulant effects, where its rhizome possesses a wide range of biologically active ingredients; such as gingerol, bisaboleneho goals, salicylate, curcumin, caffeic acid, capsaicin, zingiberene and various types of lipids (Mahmood, 2019).

Therefore, there are various medical applications owing to these medicinal properties have been researched before. These medicinal applications include; antipyretic, analgesic, antiemetic, antiulcer, cardio depressant and prostaglandins suppression (Semwal et al., 2015). Several studies showed that it has antioxidant, anti-hyperglycemic (Afshari et al., 2007), anticancer (Babasheikhali et al., 2019), anti-inflammatory (Tramontin et al., 2020), antiapoptotic (Li et al., 2020), and antihyperlipidemic actions (Kumar et al., 2013).

Moreover, Ginger has gastrointestinal protective effect as it contains several active ingredients which are known to promote digestion, absorption and counteracting constipation as well as flatulence via accelerating activity of gut muscles (Priyashantha and Mahendranathan, 2020). Ginger roots contains ingredients like Aryl alkanes that give ginger pungent taste that enhancing the appetite of animal and improve the nutrients palatability which finally caused increased feed intake (Roufogalis, 2014).

Although, the previously reviewed protective effects of ginger it had been found to produce some adverse effects. These effects include gastro intestinal upset and troubles (Zick et al., 2009). The safety and optimum dose for dietary ginger is not fully elucidated. Therefore, the target of the hereby study was to research the influence of two levels of dietary ginger on body weight, biochemical parameters, hepatic oxidative stress, gut histomorphometry and hepatic histopathology.

**MATERIAL AND METHODS**

**Animals and Treatment**

Thirty female mice weighing (18± 2 g) obtained from the Animal House of Theodor Bilharz Research Institute, Cairo, Egypt, were used for the present study. Animals were kept in standard plastic cages at the Laboratory Animal House, Faculty of Veterinary Medicine, Suez Canal University, Ismailia, Egypt. All experimental protocols were executed according to the “Guide for the Care and Use of Laboratory Animals”.

After acclimating for 14 days, mice were randomly divided into three equal groups, each containing 10 mice and treated as follows:

- **Group A (control):** served as negative control mice, fed standard rodents’ basal diet
- **Group B (Ginger 2%):** mice were fed standard rodents’ basal diet supplemented with ginger powder (Captain Co., Egypt) at rate 2%
- **Group C (Ginger 5%):** mice were fed standard rodents’ basal diet supplemented with ginger powder (Captain Co., Egypt) at rate 5%

The experimental diets were offered for 30 days.

**Body and liver weights, Feed conversion ratio (FCR) and Feed Efficiency Ratio (FER)**

Experimental mice were weighed weekly during the experimental period. The final body weight was subtracted from the initial one to obtain the weight gain. Food intake was recorded all over the thirty days of the experimental time. FCR was obtained from the formula described by Abdelrazek et al. (2018) as follows: FCR = (Feed consumption (g)/mice/30 days)/(body weight gain (g)/mice/30 days). Feed efficiency ratio (FER) was obtained from the formula described by Helmy et al. (2018) as follow:

FER = body weight gain (g) after 30 days/food intake (g) for 30 days. The liver weight was recorded then relative hepatic eight in relation to body weight was calculated.

**Sampling**

After thirty days from the start of
treatment, serum samples tissue specimens were collected from diestrus females in all groups. Mice were exposed to light tetrahydro furane anesthesia, and blood was obtained from retro-orbital plexus. The blood was let to coagulate for 20 minutes then subjected to centrifugation at 3000 rpm for 15 minutes to get the serum. The sera were kept at -20°C. After blood collection, mice were dissected and the postmortem findings were recorded; then samples from the internal organs (liver and intestine) were taken. The liver was excised, washed with ice-cold phosphate buffer saline (PBS) to remove any extraneous matter blotted to dry, and weighed, and small sections were cut. The first piece of the liver was subjected to homogenization to be applied for the antioxidant level determination. The other liver piece as well as different small intestine segments were put in 10% neutral buffered formalin for the histopathological inspection.

**Serum biochemical parameters**

Serum alanine amino transferase (ALT) and alkaline phosphatase (ALP) were measured using calorimetric Diamond Diagnostic Co., (Egypt) kits. The total protein (TP) and albumin levels were estimated in sera using calorimetric Diamond Diagnostic Co., (Egypt) kits. The level of globulin was obtained by subtracting albumin from total protein value. Albumin/ globulin (A/G) ratio was calculated.

Serum total cholesterol (TC) level, triglycerides (TGs) and high density lipoprotein cholesterol (HDLc) were determined by Spectra diagnostic, Egypt kits. The procedures were done according the enclosed kits’ pamphlet.

Liver of each experimental mice was subjected to homogenization in potassium phosphate buffer PH= 7.4. One-gram liver was added to 5 mL of the later buffer then homogenized with Teflon Homogenizer, (Spain). The samples were centrifuged at 3000 rpm at 4°C to obtain supernates. The hepatic reduced glutathione (GSH) content and malondialdehyde (MDA) as lipid peroxidation marker were estimated in supernatant using Biodiagnostic Co., (Egypt) kits.

**Histopathological examination and histochemistry**

Formalin- fixed liver and intestine were washed under running tap water, dehydrated in ascending concentration grades of ethyl alcohol and stained with H&E stain according to the standard method then examined microscopically (Slaoui and Fiette, 2011).

Other 5 μm thickness liver sections were imperiled to periodic acid Schiff (PAS) stain for glycogen according to Pearse (1968)

**Image Analysis**

Morphometric analysis for crypt depth (CD, μm), intestinal villus width (VW, μm) and villus height (VH, μm) was performed by Image J software. CD was dogged as the deepness of the invagination between two adjacent villi whereas the VH was assessed from the villus top to the lamina propria. The PAS stained liver slides were subjected to color quantification using Image J program. 5 random fields / slide/ animal were subjected to this analysis.

**Statistical Analysis**

Statistical analyses were done by the aid of SPSS software version 20.0. One-way analysis of variance (ANOVA) was used to distinguish the significant differences between the groups followed by Duncan’s multiple comparison test to find if there was any significant difference between groups. Statistical significance was deliberated when $P < 0.05$. All the values were conveyed as mean ± SE (standard error of the mean).

**RESULTS**

**Body and liver weight, FCR and FER**

The final body weight and body weight gain were significantly reduced ($P<0.05$) in mice fed with ginger 5% when matched to that of control. There were non-significant variances observed in the latter parameters in group B (Ginger 2% supplemented group) compared to control and ginger 5% fed groups.

In addition, feed intake and FER showed a significant ($P < 0.05$) decrease in ginger 5% supplemented group compared to control. However, FCR was significantly ($P < 0.05$) increased in ginger 5% supplemented group than control and 2% ginger supplemented group. Ginger 2% demonstrated significant improvement in FCR and FER than control.

Relative liver weights in group B (Ginger 2% fed mice) was significantly decreased ($P < 0.05$) in comparison to those in the control group and 5% ginger supplemented group.
Serum biochemical parameters

There were non-significant alterations in ALT levels between animals of all experimental groups. Meanwhile, the serum ALP activity was markedly decreased ($P<0.05$) in group B (Ginger 2%)supplemented mice in comparison to the control group and ginger 5% fed mice.

Interestingly, Group B (Ginger 2%) fed mice revealed a significant ($P<0.05$) elevation in total protein, albumin and globulin levels in comparison to other experimental groups.

Ginger supplementation significantly ($P<0.05$) decreased the serum total cholesterol levels in both ginger fed groups (2% and 5%) when matched to the control one. A significant ($P<0.05$) promotion in serum HDLC concentrations were noted in mice fed ginger 2% supplemented diet compared with other groups. Furthermore, TGs levels demonstrated a significant ($P<0.05$) decrease in both ginger treated groups in comparison to control ones.

Compared with control group, Ginger 2% supplementation caused significant increases in the contents of hepatic reduced glutathione (GSH). Moreover, MDA level was markedly ($P<0.05$) suppressed by ginger 2% treatment while it was significantly ($P<0.05$) increased than control in ginger 5% supplemented group.

Table 1. Effect of dietary ginger supplementation on body weight, weight gain, feed intake, feed conversion ratio (FCR), feed efficiency ratio (FER) and liver weight in female albino mice

<table>
<thead>
<tr>
<th></th>
<th>Control (group A)</th>
<th>Ginger 2% (group B)</th>
<th>Ginger 5% (group C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial body weight (g)</td>
<td>19.02±0.61</td>
<td>19.05±0.50</td>
<td>18.91±0.41</td>
</tr>
<tr>
<td>Final body weight (g)</td>
<td>27.02±1.00</td>
<td>25.05±1.00</td>
<td>22.40±1.01</td>
</tr>
<tr>
<td>Weight gain (g)</td>
<td>8.00±0.41</td>
<td>5.10±0.92</td>
<td>3.51±0.81</td>
</tr>
<tr>
<td>Feed intake (g)</td>
<td>37.81±1.10</td>
<td>30.50±2.40</td>
<td>25.6±0.7</td>
</tr>
<tr>
<td>FCR</td>
<td>5.62±0.90</td>
<td>4.01±0.31</td>
<td>9.82±1.90</td>
</tr>
<tr>
<td>Feed efficiency</td>
<td>0.21±0.03</td>
<td>0.26±0.01</td>
<td>0.10±0.03</td>
</tr>
<tr>
<td>Liver weight (g)</td>
<td>1.50±0.20</td>
<td>0.52±0.30</td>
<td>1.81±0.20</td>
</tr>
</tbody>
</table>

Different letters (a & b) indicate significant differences between interacting groups at $P<0.05$.

Table 2. Effect of dietary ginger supplementation on serum biochemical parameters, lipid profile, reduced glutathione (GHS) and lipid peroxidation (MDA) in female albino mice

<table>
<thead>
<tr>
<th></th>
<th>Control (group A)</th>
<th>Ginger 2% (group B)</th>
<th>Ginger 5% (group C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (IU/l)</td>
<td>24.40±0.21</td>
<td>24.91±0.22</td>
<td>24.30±0.14</td>
</tr>
<tr>
<td>ALP (IU/l)</td>
<td>64.41±0.32</td>
<td>60.72±1.52</td>
<td>66.52±0.84</td>
</tr>
<tr>
<td>Total protein</td>
<td>5.91±0.23</td>
<td>8.71±0.20</td>
<td>5.70±0.22</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.22±0.01</td>
<td>5.62±0.21</td>
<td>4.10±0.20</td>
</tr>
<tr>
<td>Globulin</td>
<td>1.71±0.20</td>
<td>3.10±0.20</td>
<td>1.60±0.30</td>
</tr>
<tr>
<td>A/G ratio</td>
<td>2.81±0.32</td>
<td>1.91±0.22</td>
<td>3.41±0.60</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>83.30±1.70</td>
<td>68.70±2.50</td>
<td>73.11±3.21</td>
</tr>
<tr>
<td>HDLC</td>
<td>44.71±1.51</td>
<td>54.70±1.40</td>
<td>41.71±0.91</td>
</tr>
<tr>
<td>TGs</td>
<td>83.11±0.81</td>
<td>63.42±1.71</td>
<td>71.41±4.01</td>
</tr>
<tr>
<td>GSH (mmol/g tissue)</td>
<td>25.60±1.00</td>
<td>31.10±0.50</td>
<td>22.80±1.00</td>
</tr>
<tr>
<td>MDA (nmol/g tissue)</td>
<td>0.60±0.02</td>
<td>0.50±0.01</td>
<td>0.70±0.03</td>
</tr>
</tbody>
</table>

Different letters (a, b and c) indicate significant differences between interacting groups at $P<0.05$. 
Histopathological examination and histochemistry

Stomach of control group (group A) and group B showed normal histological structure of mucosa, submucosa and serosa. Normal gastric glands, gastric pits were observed. Group C showed normal structure of all layers in addition to congestion of submucosal blood vessels. On the same hand, duodenum showed normal intact tall villi with normal enterocytes, submucosal glands and normal crypts in all examined groups. Jejunum of control group had normal long columnar villi with columnar enterocytes, while group B showed mild hyperplasia of enterocytes lining the villi and proliferation of goblet cells in group C. Examination of ileum revealed normal histological picture in all groups.

Liver of group A and B showed normal hepatic lobules, central veins and intact radiating hepatic cords around central veins. Group C had congestion of central veins along with focal aggregations of lymphocytes around the congested blood vessels. Histochemical reaction of the liver cells to PAS showed increased the positive reaction of hepatic cells of group B to PAS than other two groups.

Image Analysis

The morphometric analysis for duodenal villi height revealed significant (P<0.05) increase in VH and CD in both ginger treated groups (2% and 5%) than control however duodenal VW showed no significant differences among groups. Jejunal VH and VW revealed significant increase in ginger 2% group than control while ginger 5% treated group was non-significantly differed than control. Jejunal CD showed significant increase in both ginger 2% and ginger 5% groups than control. Ilium VH was significantly (P<0.05) increased in both ginger 2% and ginger 5% groups than control group. However, VW and CD were significantly (P<0.05) promoted in ginger 2% group than the control. Ginger 5% group showed non-significant alteration in VW and CD than control.

DISCUSSION

In the hereby study, different levels of ginger powder (2% and 5%) were added to female mice diet and their influences on final body weight, weight gain, liver weight, serum biochemical parameters, lipid profile, oxidative stress, lipid peroxidation and organ histopathology were evaluated.

The inclusion of ginger powder in diet of female mice (Ginger 2%) showed no significant variations in final weight gain as compared to control group. However, ginger 5% group (C) treated mice showed announced reduction in body weight when compared to control group (A) and ginger 2% group (B). This result was similar to Sayed et al. (2020) who reported significant decrease in body weight and weight gain after ginger administration. Moreover, food intake was observed to be significantly decreased in ginger

| Table 3. Effect of dietary ginger supplementation on intestinal morphometric analysis and liver Periodic acid Schiff (PAS) color quantification in female albino mice |
|-------------------------------------------------|-----------------|-----------------|
|                                    | Control        | Ginger 2%       | Ginger 5%       |
|                                    | (group A)      | (group B)       | (group C)       |
| Duodenum                          |                |                 |                 |
| Villus height (µm)                | 435.10±28.51   | 1280.11±52.31   | 1613.21±60.82   |
| Villus width (µm)                 | 154.30±19.20   | 126.12±25.60    | 141.42±75.61    |
| Crypt depth (µm)                  | 219.7±9.71     | 265.45±12.71    | 290.21±53.72    |
| Jejunum                           |                |                 |                 |
| Villus height (µm)                | 488.01±81.28   | 721.25±7.61     | 407.31±24.26    |
| Villus width (µm)                 | 117.11±12.55   | 278.41±14.30    | 138.13±21.51    |
| Crypt depth (µm)                  | 220.59±38.31   | 317.89±40.33    | 291.29±24.27    |
| Ilium                             |                |                 |                 |
| Villus height (µm)                | 372.75±20.96   | 656.49±19.07    | 455.33±15.02    |
| Villus width (µm)                 | 187.66±23.75   | 251.98±24.90    | 132.85±8.71     |
| Crypt depth (µm)                  | 218.48±33.51   | 249.96±37.10    | 138.43±8.10     |
| Liver                             |                |                 |                 |
| PAS staining intensity            | 55.21±3.98     | 79.32±7.89      | 45.23±5.88      |
| PAS staining area%                | 66.32±6.23     | 85.98±5.87      | 51.35±6.99      |

Different letters (a, b and c) indicate significant differences between interacting groups at P < 0.05.
5% group (C). This effect may be explained by the evidences demonstrated by several publications which stated that; many of medical herbal plants in high dose may cause reduction in food intake due to its strong bitter taste (Mansoub, 2011; Ficker et al., 2003). In our study, increasing ginger % in diet has pungent smell and taste that may attribute to the observed reduction of food intake. Also ginger at 5% level has been confirmed to reduce blood leptin level as well as fat mass (Misawa et al., 2015). Leptin has acentral part in regulation of appetite via influencing orexigenic neuropeptide Y (Kelesidis et al., 2010). Consequent to food intake reduction the FER and FCR were significantly decreased and increased, respectively in group (C). Our results concerning this point were in harmony with those obtained by Kim et al. (2018).

Ginger has a gastro protective activity and the ability to protect gastric mucosa against any necrotizing agent suggesting increased

Fig. 1. Stomach H&E staining showed normal mucosa, submucosa with normal gastric pits and gastric pits in control group (a), ginger 2% group (b) and ginger 5% group (c). Mild congestion of submucosal blood vessels (arrows) was observed in 5% ginger supplemented group (c)

Fig. 2. Duodenum H&E staining showed normal intact tall villi with normal enterocytes, submucosal glands and normal crypts in control group (a), ginger 2% group (b) and ginger 5% group (c)

Fig. 3. Jejunum H&E staining of control group (a) showed normal long columnar villi with columnar enterocytes, mild hyperplasia of villi in ginger 2% supplemented group (b) and proliferation of goblet cells in 5% ginger supplemented group (c)
digestion (Eltazi, 2014). It also stimulates digestion beneficially, enhancing the digestive activities like the intestinal lipase, the disaccharides, sucrase and maltase (Platel and Srinivasan, 1996) therefore it increased FER and reduced FCR in 2% ginger supplemented group.

Concerning the serum biochemistry results, we noticed a significant decline in serum ALT and ALP values in group B (ginger 2%). Comparatively, ginger 2% supplementation appears to exhibit higher protection of liver compared with ginger 5%. These results may be due to the existence of hepato protective natural bioactive ingredients in the ginger powder which are capable of diminishing free radical-produced liver injury (Butt and Sultan, 2011). This indicates that ginger aided in the regeneration of hepatocyte, enhanced the liver histology and function, inhibited hepatic damage, arrested further hepatic parenchymal destruction and preserved cell

---

**Fig. 4.** Ileum H&E staining showed normal histological picture in control group (a), ginger 2% group (b) and ginger 5% group (c)

**Fig. 5.** Liver H&E staining showed normal central veins, hepatic lobules and hepatocytes of control group (a) and ginger 2% group (b). Congestion of central veins (arrow heads) along with focal aggregations of lymphocytes (arrows) were observed in ginger 5% group (c)

**Fig. 6.** Liver periodic acid Schiff (PAS) histochemical stain for glycogen detection. The positive reaction was increased in hepatic cells of ginger 2% group (b) than control group (a) and ginger 5% group (c)
membrane integrity, accordingly, inhibited the enzyme release. These results came in agreement with (Patrick-Iwuanyanwu et al., 2007; Mahmoud and Elnour, 2013; Shanmugam et al., 2011).

Concerning lipid profile results, a significant reduction was observed in serum TC, TGs levels in both ginger fed groups (2% and 5%). Ginger has been confirmed to lower serum TGs and TC and raise HDLC (Misawa et al., 2015; Thomson et al., 2002; Fuhrman et al., 2000; Verma et al., 2004). It was established that ginger active ingredients could reduce cholesterol biosynthesis as well as cholesterol conversion to bile acids (Fuhrman et al., 2000). Ginger and its active contents could stimulate the activity of hepatic cholesterol-7-alpha hydroxylase, which in turn stimulates the conversion of cholesterol to bile acids, an important pathway of elimination of cholesterol from the body (Mahmoud and Elnour, 2013). Also ginger promotes fecal cholesterol excretion (Verma et al., 2004). Also, ginger can inhibit the absorption of lipids in diet by prohibiting their hydrolysis. Furthermore, (Ramakrishna Rao et al., 2003) cleared that ginger enhanced the activity of pancreatic lipase and amylase when they were directly in contact with the enzymes. Collectively, comparison between group B and group C, showed that the influence of ginger 2% treatment on reducing levels of TGs was more apparent than that of ginger 5%. The prohibiting effect of ginger on TC and TGs seen in group B and group C was consistent with previous reports that demonstrating the hypocholesterolemic and anti-atherosclerotic effects of ginger (Bhandari and Pillai, 2005; Ahmed et al., 2000; Sakr et al., 2009).

Addition of dietary ginger 2% produced significant rise in serum HDLC concentrations in comparison to the control group. HDLC is considered as protective against atherosclerosis because it moves cholesterol from marginal tissues to the liver thus serves as good transporter for plasma cholesterol (Bla ha et al., 2008).

The active constituents of ginger such as zingerone, gingerol, zingibrene, gengerols and shogos have antioxidant potential (Zancan et al., 2002). Besides, other researchers showed that ginger oils have dom inative protective effect on DNA damage induced by H2O2 and might act as a scavenger of oxygen radicals and might be used as an antioxidant (Grzanna et al., 2005).

In this investigation, hepatic GSH levels were dramatically promoted in group B (ginger 2%). These results harmonized with Mohamed et al. (2015). The possible explanation may be due to prevention of ROS generation consistent with free radical scavenging potential, omitting lipid peroxidation and protein oxidation and declined ROS-DNA interaction demonstrating the restoration of the antioxidant system of the liver (Al-Suhaimi et al., 2011).

Moreover, MDA was significantly reduced in 2% ginger supplemented group that could be seemingly linked to ginger ability to hunt reactive oxygen species particularly the most active peroxyl and hydroxyl radicals that initiated lipid peroxidation and counteract the oxidative steps (Mekuriya and Mekibib, 2018). These results were parallel to increased hepatic synthetic power of TP, albumin and globulin as well as glycogen storage in group (B). On the other side, liver content of GSH was significantly declined while MDA increased in 5% ginger supplemented group that denoted adverse effect of such dose in hepatic tissue. some researches demonstrated that increasing the dosage of herbal medicinal plants may encounter some sort of toxicity (Mansoub, 2011; Ficker et al., 2003).

Previous results were in harmony with the hepatic histopathological examination. Whereas mild histological lesions were observed in ginger 5% fed mice; including congestion in central vein as well as focal aggregation of lymphocytes. The lipid peroxidation and oxidative stress were known to be potent stimulant of hepatic proinflammatory cytokines production (Li et al., 2016; Elgawish et al., 2019) that manifested by lymphocytes aggregation. The hepatic lesion in such group was reflected on hepatic glycogen storage capacity that manifested by reduced staining area % and intensity. Consequently, the hepatic capability to synthesize TP, albumin and globulin were reduced in such group.

Gastric and intestinal histomorphometry results revealed that usage of 2% dietary ginger had more pronounced protective effect on gastric mucosa and intestinal VH, CD and CW. The later histomorphometric parameters promotion were attributed to increased digestive as well as absorption surface (Ribeiro et al., 2004) that increased the feed efficiency in current study. Contrary, administration of 5% dietary ginger produced congestion in
submucosal gastric vessels while increasing intestinal VH and CD with no alteration in VD. Other authors confirmed that higher dose of ginger could cause gastric irritation (Desai et al., 1990).

**CONCLUSION**

From the present study, it could be concluded that the incorporation of ginger in mice diet as feed additive at 2% level significantly has a great positive effect on feed efficiency, promoting blood biochemical parameters, increasing hepatic antioxidants and reduced lipid peroxidation. Along with positive change in the histological and histochemical appearance of digestive organs were observed. However, adverse effects were observed in ginger 5% dose especially concerning feed efficiency, hepatic antioxidants and hepatic histopathology as well as lipid peroxidation. Therefore, ginger should not be increased otherwise it would produce retrogressive changes or adverse effects. Further investigations using several doses of ginger must be done to elucidate an endpoint for its safe use in diet.

**Conflict of Interest**

The authors have no conflict to disclose.

**Funding Source**

This work received no external funding.

**REFERENCES**


