This study was aimed to explore the antioxidant and anti-inflammatory role of quercetin (QCT) in hydrogen peroxide (H₂O₂) treated rats. Forty (40) adult male rats were randomly divided into four groups (10 rats each) and were handled daily using gastric gavage for 30 days: Control group (C) in this group the rats were received ordinary tap water administered the vehicle only (normal saline), H₂O₂ group (T1) The rats in this group were administered orally 0.5 ml of hydrogen peroxide (H₂O₂) and given water containing 1% of H₂O₂ along experiment period (one month), H₂O₂ and Quercetin (T2) group: the animals in this group were administered orally 0.5 ml of hydrogen peroxide (H₂O₂) and given water containing one percent of H₂O₂ for 15 days followed by oral administration of Quercetin (20 mg/kg B.W) for another 15 days; Mixed (T3): group the rats were given QCT plus 1% of H₂O₂ in drinking water in the same previous doses for one month. Blood sample were collected by cardiac puncture technique at the end of the experiment and serum were collected for estimation the concentration of tumor necrosis factor -alpha (TNF-α), interleukin-10 (IL-10) and total antioxidant capacity (TOAC). After animal sacrificing, sections from small and large intestine were taken for estimation tissue reduced glutathione (GSH) and malondialdehyde (MDA) concentration. The tissue samples of intestine (Duodenum, jejunum, ileum and colon) were taken for Histomorphometric analysis (The villus height, thickness, depth of epithelial crypts and the number of goblet cell). The results showed that the oral intubation of quercetin for 15 days after H₂O₂ (group T2) or combination of quercetin and H₂O₂ for one month (group T3) caused significant decrease in TNF-α, significant increase in the IL-10 at the end of experiment comparing to the value in T1 group and the value tend to normalize that of control group. A case of oxidative stress as explained by elevation in intestinal malondialdehyde (MDA) and depression in reduced glutathione (GSH) accompanied with depression in TAOC concentration in H₂O₂ treated group comparing to QCT group which caused alleviation of pro-inflammatory and oxidative stress induced by H₂O₂. Histomorphometric analysis of intestine revealed significant elevation in depth, thickness of villus with elevation in villus height to crypt depth ratio that caused improvement in absorptive capacity of intestine, as well as elevation in number of goblet cell and some part of intestine were observed in QCT treatment groups (T2 and T3) comparing to H₂O₂ (T1) treated group. On conclusion, the current study documented, for first time, in vivo damaging effect of H₂O₂ on intestinal oxidative status, Morphometric, in addition to its effect on anti-inflammatory status. The result also pointed to protective and preventive effect of quercetin.

**Keywords**: Quercetin, intestine, oxidative status, hydrogen peroxide, IL-10.
that caused cell injury hence cell death (Kitiyanant et al., 2019). ROS generated in the body can be on several types, involving free radicals (e.g. superoxide and hydroxyl), and non-free radicals (e.g. hydrogen peroxide) (Forrester et al., 2018).

Excessive generation of ROS and H$_2$O$_2$ participate in many oxidative stress associated–diseased condition including cardiovascular disease (Ali and Khudair, 2019a), diabetes (AL-Lahhom et al., 2016), cancer (Okon and Zou, 2015), Alzheimer (Dumout and Flint, 2020), inflammatory disease (Chelomvitko, 2018), as well as hyperlipidemia and DNA damage (Ali and Khudair, 2019b).

Besides H$_2$O$_2$ and its related oxidative stress could be the major contributor to tissue injury including in vitro induced IBD (Moura et al., 2015; Patlevec et al., 2016). According to available literature, several studies concerning beneficial and damaging effect of H$_2$O$_2$ have been well studied in vitro. Yet very limited studies have concerned the detrimental effect of H$_2$O$_2$ in vivo concerning its effect on cardio vascular, hepatic, renal and reproductive system, likewise, it’s deleterious effect on intestine and as pro-inflammatory mediator has not been elucidate.

**Materials and Methods**

This study has been conducted on 40 male adult Wistar albino rats (aged 12-14 weeks and weighted 200±10g). They were adopted after acclimatization (for two weeks) in the animal house of College of Veterinary Medicine- University of Baghdad, during the period extended from November, 2019 to December, 2019. They were housed in a well-ventilated room; feed on standard pellet diet and drinking water and libitum during the experiment. The room temperature was kept at 23±2°C and 12 hrs. Light/ dark cycle along the experimental period.

After acclimatization twenty eight (28) adult male rats were randomly divided into four equal groups (7 for each) and were handled daily using gastric gavage for 30 days as follows: Control (C) group: The rats in this group were served as controls and were received ordinary tap water and administered the vehicle (normal saline); H$_2$O$_2$(T1) group: Rats in this group were drenched orally 0.5 ml of hydrogen peroxide and given tap water containing 1% of H$_2$O$_2$ along experimental period; H$_2$O$_2$ and Quercetin (T2) treated group: Rats in this group were handled as in group T1 for 15 days followed by oral administration of quercetin (20mg/kg B.W.) for another 15 days. Mixed group (T3): The rats in this group were received quercetin and H$_2$O$_2$ for one month in the same previous doses and method of administration.

At the end of experiments, rats were anesthetized by intramuscular injection of xylazine (40mg/kg B.W) and ketamine (90mg/kg B.W), then blood samples were collected via cardiac puncture technique (Para suraman et al., 2010) and serum samples were collected for measuring the concentrations of the following criteria using enzymatic kis, tumor necrosis alpha (Sunlong, China), interleukin -10 (Sunlong, China), total antioxidant capacity (Elabscience, USA).

Furthermore, tissue specimens of small and large intestine from the scarified animals were taken for estimation tissue reduced glutathione and malondialdehyde using enzymatic kit (Fine test, China). Besides, sections from whole intestine were taken for histomorphometric analysis according to (Bancroft and Marilyn, 2008). Statistical analysis of data was performed using SAS (Statistical Analysis System - version 9.1). One-way and two way ANOVA and Least significant differences (LSD) post hoc test were performed to assess significant differences among means. P<0.05 is considered statistically significant (Snedecor and Cochran, 1973).

**Results**

At the end of experiment, significant elevation (P < 0.05) in serum TNF-α concentration was observed in group T1 due to H$_2$O$_2$ for one month comparing to the value in T2, T3 and control group. On other hand, oral intubation of QCT for 15 days after H$_2$O$_2$ (group T2) or combination of QCT and H$_2$O$_2$ for one month (group T3) caused significant decrease (P < 0.05) comparing to the value in T1 group and the value tend to normalize that of control group. Within the time significant (P <0.05) decrease (T1) or increase (T2, T3) were observed at the end of experiment comparing to zero time figure (1).

![Fig. 1: Effect of Hydrogenperoxid, Quercetin and or Their Combination on Serum Tumor Necrotic Factor Alpha(TNF-α) Concentration (ng/ml) in Adult MaleRats](image-url)

Values are expressed as means ± SE, n=7. C: control group. T1: Rats administered orally 1% H$_2$O$_2$ and received water containing 1% H$_2$O$_2$ for one month. T2: Rats administered orally 1% H$_2$O$_2$ and received water containing 1% H$_2$O$_2$ for 15 days, followed by administration of 20 mg/kg B.W. Quercetin for another 15 days. T3 rats were administered orally Quercetin concurrently with 1% H$_2$O$_2$ (in same manner and dose) for one month. Different small letters denoted significant differences (P<0.05) between groups. Different capital letters denoted significant differences (P<0.05) between periods.

A significant decrease (P<0.05) in serum (IL- 10) concentration were observed in T1 (H$_2$O$_2$) group comparing to the values in control and other treated groups. Besides, oral administration of QCT after 15 days of H$_2$O$_2$ treatment in groupin (T2) group or combination of QCT and H$_2$O$_2$ (T3 group) showed significant (p < 0.05) elevation in this parameter comparing to control and T3 group (figure-2).
Values are expressed as means ± SE, n=7, C: control group. T1: Rats administered orally 1% H$_2$O$_2$ and received water containing 1% H$_2$O$_2$ for one month. T2: Rats administered orally 1% H$_2$O$_2$ and received water containing 1% H$_2$O$_2$ for 15 days, followed by administration of 20 mg/kg B.W. Quercetin for another 15 days. T3 rats were administered orally Quercetin concurrently with 1% H$_2$O$_2$ (in same manner and dose) for one month. Different small letters denoted significant differences (P<0.05) between groups. Different capital letters denoted significant differences (P<0.05) between periods.

Significant (P< 0.05) decrease in TOAC concentration were observed in H2O2 (T1) treated group which received 1% H$_2$O$_2$ for one month comparing to control, T2and T3 treated groups. On the contrary, the protective and preventive role of QCT were observed in T2, T3 after oral intubation of QCT after 15 days of H$_2$O$_2$ manipulation (T2 group) or concurrently with H$_2$O$_2$ (T3group), where significant (P< 0.05) elevation in TOAC concentration in these groups were observed comparing to H$_2$O$_2$ (T1) control group (Figure-3).

Values are expressed as means ± SE, n=7, C: control group. T1: Rats administered orally 1% H$_2$O$_2$ and received water containing 1% H$_2$O$_2$ for one month. T2: Rats administered orally 1% H$_2$O$_2$ and received water containing 1% H$_2$O$_2$ for 15 days, followed by administration of 20 mg/kg B.W. Quercetin for another 15 days. T3 rats were administered orally Quercetin concurrently with 1% H$_2$O$_2$ (in same manner and dose) for one month. Different small letters denoted significant differences (P<0.05) between groups. Different capital letters denoted significant differences (P<0.05) between periods.

Significant decrease (P < 0.05) in intestinal GSH concentration were observed after one month of treatment with 1% hydrogen peroxides figure (4) comparing to the values in control and T3. On the contrary, significant elevation (P< 0.05) in this parameter was observed after oral intubation of QCT for 15 days after H$_2$O$_2$ manipulation (T2 group), or concurrently with H$_2$O$_2$ for one month (T3 group) comparing to the value of T1 and control groups. Significant differences (P < 0.05) between T2 and T3 were also observed.
Eman Samir Aziz and Khalisa Khadhim Khudair

**Effect of Hydrogen Peroxide and Quercetin and / or their Combination on Intestinal Morphometric Analysis in Adult Male Rats**:

Table (1) illustrates different morphometric alterations in small and large intestine as following:

### Duodenum

Significant elevation (P<0.05) in depth of crypt were observed in T2 AND T3 comparing to T1 (H2O2) group, and the value in T2 is near that of control, while highest significant elevation (P<0.05) in villi thickness (VT) were observed in T2 and T3 comparing to T1 and control, while significant (P<0.05) elevation in villus height (VH) were observed in T3 group comparing to the value in other groups. Besides, the value in T2 and T3 exceed significantly (P<0.05) that of T1(H2O2) group. Highest significant elevation in VH/CD ratio was observed in T2 and control comparing to T1 and T3.

### Jejunum

Significant (P<0.05) elevation in depth of crypt were observed in T2 group, comparing to other treated group, where T1(H2O2) treated group showed Significant (P<0.05) depression comparing to other groups. Thickness of villi (VT) showed Significant (P<0.05) elevation in T2 and T3 comparing to T1 group. Significant differences (P<0.05) between T2and T3 were also observed, highest significant elevation were observed in T2 and the mean value were near that of the control. Concerning VH, Significant (P<0.05) elevation in T2 and T3 were observed comparing to T1. Highest Significant (P<0.05) elevation were observed in T3 (H2O2 and Quercetin) group. Significant (P<0.05) elevation in VH/CD ratio were observed in T1 and T3 comparing to other groups.

### Ileum

Significant elevation (P<0.05) in CD were observed in T2 and control group comparing to T3 and T1 group, where QCT intubation were given after 15 days of H2O2 exposure (T2), normalize the value to that of control. Significant elevation (P<0.05) in VT were observed in T2 group comparing value in T1 and T3 group. The result also showed that highest (P<0.05) Significant elevation in VH were observed in group T2 and T3 (QCT groups). Comparing to H2O2 (T1) group. Comparing to control, T1 and T2 group, significant elevation in VH/CD ratio were observed in T3 group.

### Colon

Significant (P<0.05) elevation in depth of crypt were observed in T2 and T3 comparing to T1 and control. Best result was clarified in T2 group. Besides, significant elevation (P<0.05) in crypt diameter were observed in T2 and T3 group comparing to T1.

### Number of goblet cell indifferent parts of small and large intestine

In duodenum significant (P<0.05) elevation in goblet cell, were observed in T2 and control groups comparing to T1 and T3 group. While in jejunum, number of goblet cell showed significant elevation in groups of control, T2 and T3 comparing to H2O2 (T1) group. The number of goblet cell in ileum showed non-Significant (P >0.05) differences in groups T1, T2 and T3 when compared to each other, and they showed significant decrease (P<0.05) as compared to control group. In colon, significant elevation in number of goblet cell were observed in T2 and T3 groups comparing to T1 and the values of these groups were near that of control (Table-1).

**Table 1**: Effect of Hydrogen Peroxide and Quercetin and / or their Combination on Intestinal Morphometric Analysis in Adult Male Rats:

<table>
<thead>
<tr>
<th>Groups</th>
<th>Depth of crypt (CD) (µm)</th>
<th>Thickness of villi (TH) (µm)</th>
<th>Villus High (VH) (µm)</th>
<th>VH/CD ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Duodenum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>89.02±4.50b</td>
<td>53.48±2.48b</td>
<td>262.35±6.59b</td>
<td>2.97±0.10a</td>
</tr>
<tr>
<td>T1</td>
<td>72.37±2.37c</td>
<td>35.94±1.15c</td>
<td>175.82±7.52d</td>
<td>2.44±0.13b</td>
</tr>
<tr>
<td>T2</td>
<td>89.51±2.59b</td>
<td>62.31±2.58a</td>
<td>231.07±5.27c</td>
<td>2.59±0.11b</td>
</tr>
<tr>
<td>T3</td>
<td>100.57±2.46a</td>
<td>63.08±3.41a</td>
<td>312.19±4.39a</td>
<td>3.11±0.05a</td>
</tr>
<tr>
<td>LSD</td>
<td>9.1766</td>
<td>7.4954</td>
<td>17.91</td>
<td>0.3068</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Jejunum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>75.86±2.43b</td>
<td>55.38±3.22a</td>
<td>188.99±20.34bc</td>
<td>2.53±0.32bc</td>
</tr>
<tr>
<td>T1</td>
<td>55.73±3.99c</td>
<td>38.00±2.36c</td>
<td>170.06±5.28c</td>
<td>3.15±0.29ab</td>
</tr>
<tr>
<td>T2</td>
<td>101.66±3.03a</td>
<td>59.50±2.73a</td>
<td>213.61±6.95b</td>
<td>2.11±0.11c</td>
</tr>
</tbody>
</table>
Ameliorative role of quercetin on intestinal histomorpometric, oxidative status and pro-inflammatory changes in hydrogen peroxide–exposed rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>Depth of crypt</th>
<th>Diameter of crypt</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>118.59±0.61c</td>
<td>54.85±1.29a</td>
</tr>
<tr>
<td>T1</td>
<td>119.56±2.84c</td>
<td>36.50±1.75c</td>
</tr>
<tr>
<td>T2</td>
<td>167.59±4.64a</td>
<td>50.36±2.35ab</td>
</tr>
<tr>
<td>T3</td>
<td>153.00±6.44b</td>
<td>49.32±1.56b</td>
</tr>
<tr>
<td>LSD</td>
<td>12.485</td>
<td>5.2657</td>
</tr>
</tbody>
</table>

Number of goblet cell / cells/2000μm²

<table>
<thead>
<tr>
<th>Groups</th>
<th>Duodenum</th>
<th>Jejunum</th>
<th>Ileum</th>
<th>Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>3.50±0.34a</td>
<td>3.16±0.16a</td>
<td>3.58±0.20a</td>
<td>4.91±0.27a</td>
</tr>
<tr>
<td>T1</td>
<td>2.00±0.25b</td>
<td>2.08±0.27b</td>
<td>2.08±0.27b</td>
<td>3.41±0.20b</td>
</tr>
<tr>
<td>T2</td>
<td>3.66±0.21a</td>
<td>3.08±0.32a</td>
<td>2.66±0.21b</td>
<td>4.50±0.76a</td>
</tr>
<tr>
<td>T3</td>
<td>2.58±0.20b</td>
<td>3.08±0.27a</td>
<td>2.50±0.34b</td>
<td>4.50±0.76a</td>
</tr>
<tr>
<td>LSD</td>
<td>0.7637</td>
<td>0.7832</td>
<td>0.7735</td>
<td>0.6691</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE, n=7, C: control group. T1: Rats administered orally 1% H2O2 and received water containing 1% H2O2 for one month. T2: Rats administered orally 1% H2O2 and received water containing 1% H2O2 for 15 days, followed by administration of 20 mg/kg B.W. Quercetin for another 15 days. T3 rats were administered orally Quercetin concurrently with 1% H2O2 (in same manner and dose) for one month. Different small letters denoted significant differences (P<0.05) between groups.

Antioxidant status

The result in current study revealed that oral administration of QCT for thirty days caused significant decrease in intestinal MDA and elevation in intestinal GSH concentration comparing to H2O2 and mixed groups. Quercetin is regarded as powerful free radical scavenger and prevention of lipid peroxidation in vitro (Chen et al., 2018), as well as Quercetin antioxidant effects in serum and different organs has been reported (Degroote et al., 2019). Ren and his colleagues (2018) recorded that QCT protected andameliorate against oxidative stress and injury induced by H2O2 in colonic epithelium and QCT was found to alleviate the depression of intracellular GSH concentration caused by H2O2 (Donget al., 2020).

Dietary Quercetin supplementation has protective effect on intestine manifested by elevation in GSH -PX, SOD and decrease level of MDA, which indicated improvement in intestinal oxidative stress (Van Le Thanh et al., 2016). Experimentally induced colitis model, showed decreased in GSH level and this can be re stored to normal level by antioxidant Quercetin as all flavonoids promote translocation of Nrfr from cytoplasm to the nucleus and activating Nrfr signaling pathway (Baharetal, 2017) and then prevent mitochondria dysfunction and oxidative stress. A study reported that QCT ameliorate oxidative stress biomarkers such as myeloperoxidase and MAD (Hong and Piao, 2018), and the mechanism could be amelioration of T-cell mediated colitis by modulating the(HO-1) formation (Ju et al., 2017). Besides, improved expression of glutamate cysteine ligase (GLC) catalytic subunit, a firstrate limiting enzyme of GSH synthesis, and elevation of intracellular GSH concentration by QCT (Patlevic et al., 2016) treatment accompanied withamelioration excessive ROS production and lipid peroxidation (MDA) product has been documented (Wiegand et al., 2009).

Another mechanism for intestinal GSH elevation by QCT could be though down regulation the transcription of AOP3, an H2O2 transporting protein present in the cell membrane that facilities uptake of H2O2 (Thiagarajah et al., 2017), in H2O2 exposed cell (in vitro) caused depression in intracellular H2O2 and elevated GSH (Dong et al., 2020). Flavonoids compounds such as Quercetin are characterized by presences of one or more phenol ring and two or more hydroxyl groups linked directly to aromatic ring (Cutillo et al., 2006), have been associated with their anti - proliferative, anti-inflammatory and antioxidant properties (Sarkar et al., 2016).

Concerning the effect of H2O2 on intestinal antioxidant status, the current study showed significant elevation in intestinal MDA and decrease in intestinal GSHin H2O2 treated group. At low level, ROS including H2O2 were essential for cell differentiation ion ,apoptosis and function as second messenger, however, an elevation in H2O2 and induction ofoxidative stress, decreased intra cellular GSH and or decrease MDA level has been documented in vitro (Dong et al., 2020). Besides, H2O2 caused reduction in GSH level in serumand in different organs has been documented in vivo (Khudair, 2010).

Malondialdehyde (MDA), is a cytotoxic products (biomarkers of LPO), has been associated with pathogenesis of IBD and colon cancer (Naira et al., 2007). Its elevation by H2O2 and depression in GSH indicated case of oxidative stress and inflammation (Bhattacharyya et al., 2014). Over production of ROS and elevated formation of H2O2 results in lipid peroxidation (LPO), protein oxidation, DNA damage &induced intestinal damage (Rezai et al., 2015) and disruption of intestinal barrier (Aw et al., 2005), where ROS induced intestinal epithelia cell damage has been associated.
with pathogenesis of inflammatory bowel disease including cohan disease and ulcerative colitis (Rezaei et al., 2015)

**Anti-inflammatory status**

In the current study, significant decrease in serum TNF-α and elevation in serum IL-10 concentration was observed in QCT treated group, indicated its anti-inflammatory effects, which was documented by many investigators in vitro (Nikfarjam et al., 2017) and in vivo (Egert et al., 2009). One of the most remarkable properties of QCT is its ability to modulate inflammation. It inhibit cyclooxygenase and lipoxygenase pathway thereby decreasing inflammatory mediators such as prostaglandins and leukotriens (Lee et al., 2010). Quercetin has been used in patients with neutrophil mediated inflammatory disease (Nikforjam et al., 2017) and inhibit production of pro inflammatory cytokines such as IL-6 and TNF-α from macrophage in lipopolysaccharide induced inflammation (Huang et al., 2015). Besides, Quercetin anti-inflammatory properties in relation to obesity and type-2 diabetes is documented (Chen et al., 2016).

Fiedles and his colleagues (2020) demonstrated that quercetin 3-Rutinord possess anti-inflammatory, cytoprotective and gastro protective activities, which was attributed to suppression of TNF-α, IL-6 and blocking activities of nuclear factor kB (NFkB) transcription and promote expression of inflammatory cytokines (Lee et al., 2018). Quercetin may be the best flavonoids candidates to provide anti-inflammatory reflex in vivo, attributed to their inhibitory effect on TNF-α and iNOS synthase expression coupled with enhancement of IL-10 release (Comalada et al., 2005).

Besides, the reduction of TNF-alpha by QCT may be though down regulation significantly myeloperoxidase as activity, which is indicative of decrease neutrophil infiltration and thereby reduced generation of ROS (Toth et al., 2017). On conclusion, the use of QCT in H₂O₂ exposed rats, prevent intestinal damage and enhance intestinal recovery via oxygen radical scavenger activity, nitric oxide and xanthan oxidase inhibition, lipid oxidation inhibition & metal chelating activity (Leyva et al., 2016).

In the current study, significant elevation in serum TNF-α and depression in serum IL-10 was observed in H₂O₂ (T2) treated group comparing to other treated groups which is attributed to inflammatory status. The pro-inflammatory effect of H₂O₂ was documented in vitro through increased expression of COX2, inflammatory cytokines, such as TNFα, IL-6 (Okoko, 2018) and pro inflammatory transcription factor NF-kB (Gupta et al., 2012). Hydrogen peroxide could be produced by lymphocyte, monocyte and neutrophil that coming from leukocyte infiltration which is characteristic features of intestinal inflammation (Moura et al., 2015). Besides, ROS (to which H₂O₂ is belong) coordinate the inflammatory response of tissue (Nrethammer et al., 2009), where TNF-alpha is central mediator of inflammation (Oncel et al., 2016).

The redox sensitive -nuclear-factor-erythroid-2 related factor-2 (Nrf2) transcription factor, is the main defense mechanism against various harmless stress, it improves the bodd oxidative status and maintain cellular redox homeostasis (Hafezet al., 2019). Reactive oxygen species (H₂O₂) may cause decrease in expression of this cytoprotective (Nrf2) factor (Mouetal, 2019), leading to oxidative stress (Pickering et al., 2013) and decrease in anti-inflammatory response that may be accompanied with depression in TNF-alpha and IL-10 concentration.

An association between IL-10, a key anti-inflammatory cytokines, and intestinal mucosal homeostasis is documented, where IL-10 and its’ receptors signaling modulate innate and adaptive immune response in GIT and play role in inhibition of upregulation of inflammation & oxidative stress (Cheng et al., 2018) and prevention of IBD (Shouval et al., 2014). Depression of this interleukins by H₂O₂ indicating a case of inflammation. Besides, H₂O₂ activates the release of high morbidity group -1 protein from macrophages, resulting in amplification of pro inflammatory stimulation (Sies et al., 2017) could be a mechanism.

**Morphometric changes**

The optimal gut health is characterized by several ways, one of which is villus height, crypt depth ratio, a high ratio indicated maturend well-functioning villi, with shallowcrypt, that is constantly providing cell renewal (Cuie et al., 2020).

The intestinal histomorphological parameters measurement in groups T2 and T3 showed significant elevation in VH and CD, suggested improvement of absorptive and digestive capacity of small intestine (Zhang et al., 2020) which could be a mechanism for QCT. Besides, an elevation in morphometric and physiological performance of intestinal mucosa such as VH and number of goblet cell by QCT, could be through elevation of mucosal proliferation , differentiationand enzymatic activity (Sun et al., 2020).

The improvementfobovementioned criteria by QCT could be through stimulation activity of probiotic bacteria associated with elevationin short chain fatty acidmainlybutyric acidthat participate in elevation intestinal absorption and digestion capacity (Yadava and Jha, 2019).

As we, an elevation in length of absorptive surface in determined by villus height and crypt depth, where elevation in villus height score indicated an elevation in absorption capacity and healthyand well developed small intestine (Cui et al., 2020). Accordingly, depression in these morphometric criteria by H₂O₂ indicated decreased absorptive capacity of intestine, besides, the measurement of villus are correlated very well with total number oepithelialiccell in villus (Krndija et al., 2019).

Histomorphometricalalterations, such as decreased in villus height, crypt necrosisand inflammatoryinfiltrationare reportedin H₂O₂ treated groups. H₂O₂ treated rats showed severe, atrophy epithelia flatting, extensive crypt loss in vitro (Sukhotnik et al., 2018).

As we previously mentioned, An elevationin VH/CD ratio result in slowturnover of intestinal mucosa, that could result in higher growth efficacay of animal (Parker et al., 2019).

Depleted in goblet cell number in H₂O₂ treated rat, indicated a case of inflammation and ulceration colitis associated with low mucin secretion that damage epithelial tight junction leading to inflammation (Lin et al., 2016) which could be related to inhibition of probiotic bacteria and decrease in pathogenicbacteria, accompanied with decreased in fermentationand loweringof shortchain fatty acid production (akey anti-inflammatory metabolitesinduced by commensal bacteria) (Chen et al., 2019) leading to
pathogenetic change in histopathological picture of intestine. On the contrary, another research reported that exposure to stress developed an adaptation mechanism characterized by elongation in villus and deepening of crypt which increases absorption capacity and digestion/unit length (Cormula et al., 2019).

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