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The Effect of Cinnamon to the Expression of SOD-1 and TNF-\(\alpha\) in Indomethacin-Induced Gastric Ulcer Rat

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Abstract. Gastric ulcer is a disease that commonly occurs and spreads over the world, and one of the most common causes is the use of long-term non-steroid anti-inflammatory drugs (NSAIDs). Active compounds of bark and leaves of the cinnamon extract are cinnamaldehyde and eugenol, which are acting as gastroprotective by antioxidant and anti-inflammatory properties and also flavonoids such as quercetin, kaempferol, and quercetrin as an antioxidant. This study aimed to determine the effect of cinnamon extract on the expression of SOD-1 and TNF-\(\alpha\) in indomethacin-induced gastric ulcers. Indomethacin 30 mg/kg BW orally induced after 8 hour fasting period. Cinnamon extract administered in different doses daily for two days. The rats divided into 6 groups: negative control group, positive control group on first day, positive control group on third day, and three treatment groups (T1, T2, and T3) with cinnamon extract doses of 400, 200 and 100 mg/kg BW respectively. The level of SOD-1 measured by ELISA and the expression of TNF-\(\alpha\) by immunohistochemistry from gastric mucosa. The results showed that cinnamon extract significantly increased SOD-1 and decrease of TNF-\(\alpha\). Histopathology analysis showed the improvement of gastric epithelial after cinnamon provision. These results demonstrate that the administration of cinnamon extract may protect indomethacin-induced gastric ulcer rats through their antioxidant and anti-inflammatory properties, and also it is improving gastric histopathology.

INTRODUCTION

A gastric ulcer is a sore or hole in the lining of the stomach, and it is a mucosal defect that reaches the muscularis mucosa. Due to its high morbidity, mortality, and economic loss, peptic ulcer become a worldwide health problem [1]. A gastric ulcer (also known as peptic ulcer) is a chronic development which is characterized by an imbalance between aggressive factors such as NSAIDs, reactive oxygen species (ROS), gastric acid, pepsin, and defensive factors such as antioxidants, bicarbonate, mucosal blood flow, mucus, and prostaglandins [2, 3].

NSAIDs can cause gastric ulcers by inhibiting the synthesis of prostaglandins (PGs) from arachidonic acid by inhibiting cyclooxygenase enzymes (COX-1 and COX-2) that lead to a deficiency of prostaglandin E2 (PGE2) and able to inhibit the ulcer healing process. Lack of PGE2 leads to oxidative stress and the production of free radicals [4]. Reactive oxygen species (ROS) which cause lipid peroxidation and play a critical role in the development of pathogenesis of gastric damage induced by NSAIDs. When ROS attack to cells, the cells defend themselves using radical scavenging enzymes such as SOD [5]. Superoxide dismutase is the the most potent antioxidant in the cell and as fist defence of the cell through the free radicals attack. It catalyzes the superoxide anion (O\(^2^-\)) to molecular oxygen.
(O₂) and hydrogen peroxide (H₂O₂). The conversion of H₂O₂ follows it into a water molecule by another enzyme-like catalase and peroxidase [6, 7].

Tumor necrosis factor-α (TNF-α) is pro-inflammatory cytokine exhibiting various effects on many cell types and play a critical role in the pathogenesis of chronic inflammatory diseases and also involved in the regulation of different physiological and pathological processes (proliferation, apoptosis, differentiation, and modulation of immune response. Neutrophils produce TNF-α, activated T and B lymphocytes, endothelial cells, smooth muscle cells, but mainly produced by activated macrophages [8, 9].

The drugs are expensive for certain people and have many side effects. Therefore, the health-promoting and disease-preventing properties from a plant-derived compound such as cinnamon is developed. Cinnamon known has well tolerated, and gastrointestinal side effects are common, which are self-limiting in the majority of cases, especially with large doses or longer duration [10, 11]. Cinnamon is a common spice used around the world for several centuries. Its gain from the inner bark of genus Cinnamomum and family Lauraceae, which have used as a popular spice, condiment, and flavoring. It is obtained from every part of the cinnamon tree, including the bark, flowers, fruits, leaves, and roots [12]. Cinnamon is a traditional herb used for many diseases such as diabetes mellitus, hyperlipidemia, arthritis, and it also has effect as an antioxidant, anti-inflammatory, anti-spasmodic, anti-ulcerative, anti-bacterial, anti-septic, anti-lipemic, anti-tumor, anti-diabetic, hepatoprotective and anti-mutagenic [10, 13].

Hence, this study aim was to explore the possible antioxidant and anti-inflammatory effect of cinnamon extract on gastric ulcer-induced by indomethacin by looking at SOD-1 and TNF-α expression in rat gastric mucosa.

**EXPERIMENTAL DETAILS**

**Subject**

Male Wistar rats (150-200 g), 7-8 weeks old, obtained from the department of pharmacology at the Universitas Brawijaya were used in this research. The animals were maintained on a standard pellet diet and tap water and also under healthy conditions of humidity, temperature (20-25 °C) and light (12-h light: 12-h dark cycle). The study was conducted according to the guidelines of the Animal Ethics Committee of Faculty of Medicine Universitas Brawijaya.

**Materials**

Indomethacin was obtained from Sigma pharmaceutical company, Catalog No: 17378. SOD-1 ELISA kit was obtained from Bioassay Technology Laboratory, Catalog No: E4502Hu, Shanghai, China. TNF-α immunohistochemistry kit was obtained from Santa Cruz Biotechnology, Catalog No: 52B83, Inc, USA.

**Preparation of Cinnamon Ethanolic Extract**

The extraction of cinnamon was done in the pharmacological department of the Faculty of medicine in Universitas Brawijaya, Malang, Indonesia. The powder of cinnamon (Bark and Leaves) was from Materia Medica, Batu, Indonesia. The material was weighed 100 g, soaked with ethanol of 900 mL to 1 Liter Erlenmeyer. The mixture was shaken for 30 minutes, soaked overnight. The top layer of the mixture, which is a mixture of solvents and active substances was taken and put into the evaporation flask. The evaporation process was carried out at a temperature of 70 °C until the solvent flow stopped dripping on the pumpkin container. Results of the extraction put in glass or plastic bottles and stored in a freezer.

**Indomethacin-induced Gastric Ulcer**

The experimental animals were fasted for 8 hours without being fed but allowed to drink, then positive control group on the first day, positive control group on the third day, and treatment groups (T1, T2, and T3) were given indomethacin orally for induction of gastric ulcer at dose of 30 mg/kg bw [14]. Experimental models of gastric ulcer in the positive control group on the first day were sacrificed by cervical dislocation on the first day. The positive control group on the third day was left alive and received at libitum food and drink. The treatment groups T1, T2, and T3 received the cinnamon extract 8 hours after indomethacin administration with doses 100 mg/kg, 200 mg/kg, and 400 mg/kg body weight, respectively [15]. Administration of cinnamon extract was continued for two days (twice
only) with a frequency of 1x/day. The negative control group, positive control group on third day, and treatment groups (T1, T2, and T3), were sacrificed by cervical dislocation 24 hours after the last cinnamon extract administration.

**Histological Preparation**

Gastric tissue were gain from each group were fixed in 10% formalin for 24 hours. The specimens were embedded in paraffin block and slicing (3- 5 mm) then stained by Hematoxylin and Eosin The histological sections were observed by light microscope and photographed (100x magnification). One experienced histopathologist examined all samples for histopathological findings.

**Data Collection**

One day after the last dose of giving drugs, the rats were sacrificed by cervical dislocation. The gastric tissue was obtained from rats and washing well with normal saline. Pyloric part of stomach was storage at – 80 °C until measurement of SOD-1 by ELISA kit in Biomedical Laboratory, then rinse gastric tissue in PBS (PH 7.4) to remove excess blood thoroughly and weigh before homogenization, after that mince tissue and homogenize them in PBS (PH 7.4) with a glass homogenize on ice and thaw at 2-8 °C or freeze at 20 °C and centrifuge at 2000-3000 RPM for approximately 20 minutes, finally the measurement expression of SOD-1 by ELISA kit. Fundic part of stomach was placed in the bottle containing formalin 10% and sent for immunohistochemistry to analysis the expression of TNF-α, then calculation of TNF-α expression in epithelial cells was conducted by seeing the presence of brown color in the cytoplasm of staining cells by looking at slide under the microscope, observation was done by calculating the cells that are observed in 20 fields of views with magnification of 400x by DAB/nuclear area percentage calculated with immune Ratio program.

**Data Analysis**

The result data from this research was analyzed statistically with one-way analysis of variance (ANOVA) using SPSS 16.0, followed by the post hoc test of multiple comparisons. A probability value of P < 0.05 was considered to be significant. Pearson correlation test was performed to find out the vital relationship between different doses of a cinnamon extract with an expression of SOD-1 and TNF-α.

**RESULTS AND DISCUSSION**

**Ethanolic Extract of Cinnamon Increased Expression of SOD-1 in Gastric Ulcer-induced by Indomethacin in Rats**

This study showed that Indomethacine decreased SOD level significantly, and the ethanol extract of cinnamon was able to increase the expression of SOD-1 in gastric mucosa of rats (P= 0.000). As for the overall differences in the expression of SOD-1 in each treatment, groups can also be depicted in Fig. 1.

Based on Figure 1 shows that the difference in doses of the cinnamon extract has a different effect on the expression of SOD-1 in gastric ulcer-induced by indomethacin in the rat. The existence of the effect of cinnamon extract is starting to look where the expression of SOD-1 in gastric ulcer-induced by indomethacin in rat becomes higher after the treatment was given in the form of cinnamon extract started with a dose of 100 mg/kg, compared with the expression of SOD-1 in positive control groups. Furthermore, the expression of SOD-1 increased when they were given higher doses of cinnamon. Thus, based on the assessment descriptively according to the means of the expression of SOD-1, it can be said that administration of treatment in the form of cinnamon extract at doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg showed difference effect, where the higher dose of cinnamon extract provided further increasing of the expression of SOD-1. However, the dose of 100 mg/kg is the most likely effective dose because of the expression of SOD-1 near to its expression in the negative control group. The expression of SOD-1 in the C+1ST day group differs significantly with the expression of SOD-1 in C+3rd day group, T1 group, T2 group, and T3 group (P-value < 0.05). The expression of SOD-1 in C+3rd day group differ significantly with the expression of SOD-1 in C+1ST day group, T2 group, and T3 group (P-value < 0.05), and expression of SOD-1 in C+ 3rd day group did not differ
significantly with expression of SOD-1 in C- group and T1 group (P-value > 0.05). The expression of SOD-1 in the T1 group differs significantly with the expression in C+ 1st group and the T3 group (P-value < 0.05). The expression of SOD-1 in the T2 group differs significantly with the expression in C- group, C+1st group, C+3rd, and T3 group (P-value < 0.05). The expression of SOD-1 in the T3 group differs significantly with the expression in C- group, C+1st group, C+3rd group, T1 group, and T2 group (P-value < 0.05).

FIGURE 1. The expression of SOD-1 at each group. The expression of SOD-1 in C+ groups (1st and 3rd) is lower than expression in C- group. In the treatment groups, the expression of SOD-1 is different, but T1 is near to C-. T1=Cinnamon extract 100 mg/kg BW, T2 = Cinnamon extract 200 mg/kg BW, T3= Cinnamon extract 400 mg/kg BW

Cinnamon extract at a dose of 400 mg/kg can increase the expression of SOD-1 more than the provision of cinnamon extract at a dose of 200 mg/kg. So the dose of 400 mg/kg of cinnamon extract was more useful to increasing the expression of SOD-1 than at a dose of 200 mg/kg of cinnamon extract and also the provision of cinnamon extract at a dose of 200 mg/kg is more expression of SOD-1 than at a dose of 100 mg/kg of cinnamon extract. Based on the results of the correlation test, there was a correlation between the different doses of cinnamon extract and the expression of SOD-1 have a coefficient of correlation equals to 0.924, which means the relationship is quite strong, that means increasing the dose of cinnamon extract will be followed by increasing the expression of SOD-1.

Ethanolic Extract of Cinnamon Decreased Expression of TNF-α in Gastric Ulcer-induced by Indomethacin in Rats

This study showed that the ethanol extract of cinnamon was able to decrease the expression of TNF-α in gastric mucosa of rats (P= 0.000). As for the overall differences in the expression of TNF-α in each treatment, groups can also be depicted in Fig. 2.

Based on Figure 2 shows that the difference in doses of the cinnamon extract has a different effect on the expression of TNF-α in gastric ulcer-induced by indomethacin in the rat. The existence of the impact of cinnamon extract is starting to look where the expression of TNF-α in gastric ulcer-induced by indomethacin in rat becomes lower after the treatment was given in the form of cinnamon extract started at a dose of 100 mg/kg, compared with expression of TNF-α in the positive control group. Then the expression of TNF-α decreased when they were given higher doses of cinnamon. Thus, based on the assessment descriptively according to the means of expression of TNF-α, it can be said...
the administration of treatment in the form of cinnamon extract at a dose of 100 mg/kg, 200 mg/kg, and 400 mg/kg showed different effect, where the higher dose of cinnamon extract provided further decreasing of the expression of TNF-α. The expression of TNF-α in the C- group differs significantly with the expression in the C+1st group, C+3rd group, T1 group, T2 group, and T3 group (P< 0.05). The expression of TNF-α in the C+1st group differs significantly with expression in C- group, C+3rd group, T1 group, T2 group, and T3 group (P<0.05). The expression of TNF-α in the C+3rd group differs significantly with expression in C- group, C+1st group, and C+3rd group (P<0.05). The expression of TNF-α in the T1 group differs significantly with expression in C- group, C+1st group, and C+3rd group (P<0.05). The expression of TNF-α in the T2 group differs significantly with expression in C- group, C+1st group, and C+3rd group (P<0.05). The expression of TNF-α in the T3 group differs significantly with expression in C- group, C+1st group, and C+3rd group (P<0.05). The result of the expression of TNF-α by immunohistochemistry is depicted in Fig. 3.

![Fig. 3](image)

**FIGURE 2.** The expression of TNF-α at each group. The expression of TNF-α in C+ groups (1st and 3rd) is higher than in C- group. In treatment groups, the expression of TNF-α is different, but in T1 is near to C- group. T1=Cinnamon extract 100 mg/kg BW, T2 = Cinnamon extract 200 mg/kg BW, T3= Cinnamon extract 400 mg/kg BW

Administration of the cinnamon extract at a dose of 400 mg/kg can decrease the expression of TNF-α lower than the provision of cinnamon extract at a dose of 100 mg/kg or 200 mg/kg. So the dose of 400 mg/kg was more useful to decrease the expression of TNF-α than the dose of 200 mg/kg and also provision of cinnamon extract at a dose of 200 mg/kg is lower expression of TNF-α than at a dose of 100 mg/kg of cinnamon extract. Based on the result of correlation test, there was a correlation between the different doses of the cinnamon extract with the expression of TNF-α have a coefficient of correlation equals to -0.795, which means the relationship is quite strong, that means the increasing the doses of cinnamon extract will be followed by decreasing the expression of TNF-α.
Hematoxylin and eosin were used for histological staining to evaluate the stomach histology. The histochemical sections were evaluated by light microscope and photographed (100x magnification). One experienced histopathologist examined all samples using a light microscope. Histopathological finding as to the following:

- All gland cells, gastric epithelial cells, parietal, and the chief cells had typical histological structures in the stomach samples of the negative control group (Fig. 4A).
- In control positive on the first day showed gastric epithelial ulceration, severe cellular losses, submucosal edema, and congestion of submucosal blood vessels and infiltration of inflammatory cells (Fig. 4B).
- In control positive on the third day showed reduced gastric epithelial ulceration and epithelial losses, and also decreased submucosal edema compared with control positive on the first-day group (Fig. 4C).
- In treatment groups (1, 2, and 3) with cinnamon extract at doses of (100, 200, 400 mg/kg BW), respectively, had typical histological structures in the stomach samples (Fig 4D, E, and F).

The administration of non-steroidal anti-inflammatory drugs (NSAIDs) in this study was conducted by using indomethacin at a dose of 30 mg/kg and was able to cause gastric ulcers because of prostaglandin (PG) deficiency by cyclooxygenase (COX-1 and COX-2) inhibition [16]. Furthermore, prostaglandin deficiency caused gastric hypermotility, decreased blood flow in the gastric mucosa, decreased mucous layer formation, bicarbonate and phospholipid, increased mucosal permeability, and increased acid production. This results in the activation of inflammatory mediators, impaired repair, and healing of the mucosa, forming a gastric ulcer. The process began with an increase in growth factors, such as base fibroblast growth factor (bFGF). bFGF is expressed by healthy gastric tissue in both mice and humans, and it was reported that its expression increased when gastric ulcer occurred [14].

Deficiency of prostaglandin E2 (PGE2) lead to leukocyte-endothelial interaction, which causing production of ROS that causing gastric damage because prostaglandin E2 has strong cytoprotective effect on gastric mucosa including increased epithelial mucus production, increased bicarbonate secretion, inhibition of gastric motility, inhibition of acid secretion, improvement of mucosal blood flow and repression of free radicals and enzymes release from neutrophil [17]. The first line of mucosal defense is adequate secretion of bicarbonate and mucosal blood flow with the formation of an alkaline buffer layer at the epithelial surface. PGs are involved in the ulcer healing process [18]. PGE2 stimulates the growth factors such as epidermal growth factor (EGF). The epidermal growth factor participates in gastroduodenal protection and healing of gastric ulcers by stimulating angiogenesis, granulation tissue formation, and re-epithelialization [19].
The damage of mucus, phospholipid layer, bicarbonate exfoliation of the surface epithelial thus its loss of barrier, and the capillary endothelium was damaged caused microvascular stasis with the cessation of oxygen and nutrient delivery. During early mucosal injury, microvascular damage can occur, that led to necrosis of epithelial cells and hypoxia. Pro-inflammatory mediators from injured cells released vasoconstriction from macrophages, and endothelial cells that ameliorate the mucosal microcirculation necrosis. Ulcer healing is resulted from many process of repairing mucosal defect with connective tissue cells, cell proliferation, migration, regeneration, differentiation, active angiogenesis, and extracellular matrix deposition and epithelial cells. Growth factors, including EGF and PGE2 involved in process of re-epithelialization and gland re-construction is controlled by, which are triggering cell proliferation [20].

The balance between ROS and antioxidant defense needed to eliminate oxidative stress [21]. Both exogenous and endogenous antioxidants are used to scavenged free radicals and protect cells from free radicals by maintaining redox balance. Antioxidant Superoxide dismutase (SOD) is an essential endogenous antioxidant enzyme, that could scavenges superoxide radicals. Catalase antioxidant reveal the dismutation of superoxide radical (O$_2^-$) to oxygen and hydrogen peroxide (H$_2$O$_2$) [22].

NSAIDs decrease the PGE2 level, which causes an elevation of TNF-α. TNF-α, a pro-inflammatory cytokine, plays a vital role in the expression of iNOS or Type II NOS. iNOS is the main enzyme in NO production. NO is another significant mediator of inflammation. It leads to tissue injury.

Furthermore, TNF-α stimulates the ICAM-1 expression on the endothelium. ICAM-1 directly related to an increase of neutrophil adhesion. ICAM-1 also induces transendothelial migration of leukocytes to the inflamed tissue, which also results in more tissue damage. Besides, TNF-α stimulates NF-κB causes gastric injury through various pathways. First, NF-KB increases inflammatory cytokines synthesis such as IL-1, IL-6, and IL-8 and increase these inflammatory cytokine receptors. Second, NF-KB regulates adhesion molecules such as ICAM-1 expression. Neutrophil accumulation and adhesion stimulated by various inflammatory cytokines will lead to tissue damage [23].

From previous study showed clearly the cinnamon aqueous suspension had antiulcerogenic properties because the suspension contains substances that might enhance endogenous prostaglandins, mucus synthesis and possess antioxidant properties (potentiation of defense factors) and aqueous suspension of cinnamon showed a significant

FIGURE 4. Histopathological Finding of the gastric mucosa of the rats in each group. (A) Negative control group showing healthy gastric mucosa appearance, (B) positive control group on the first day showing gastric epithelial ulceration, intense cellular loss, submucosal edema (The arrow indicating to submucosal edema) and congestion of submucosal blood vessels and infiltration of inflammatory cells, (C) positive control group on the third day showing reduced gastric epithelial ulceration and decreased submucosal edema compared with control positive of the first-day group, and treatment groups (D, E, and F) with doses of cinnamon (100, 200, and 400 mg/kg) respectively showing typical histological structures of gastric mucosa. Hematoxylin and Eosin stain with 100x magnification.
Inflammation process is needed to protect for removal the effect of harmful substances produced by injurious stimuli. Oral administration of cinnamon water extract to mice was reported significantly decreased the serum level of TNF-α and IL-6 indicating that anti-inflammatory compounds of cinnamon extract may originate from the presence of polyphenols [25]. In another study, showed that cinnamon and chamomile aqueous extract at different doses (100, 200, 300, 400 mg/kg b.w) had a gastroprotective effect on gastric ulcer in rats [15]. Increased SOD and CAT levels of gastric mucosa were found in the oleum cinnamomi treated ulcerative stomach because of antioxidant properties of oleum cinnamon, which protected the gastric mucosa against ethanol toxicity and reduced the mucosal damage [11]. The intraperitoneal administration of an aqueous extract of cinnamon cassia to rats at a dose of 100 mg/kg b.w prevented the occurrence of stress ulcer exposure to cold atmosphere 3-5°C or on restraint in water 22- 24°C. It also strongly inhibited gastric ulcers induced by subcutaneous injection of serotonin in rats [26].

Eugenol is a phenolic compound and used in the food industry as a preservative, because of its antioxidant property, it can also be found in soybean, bean, coffee, and cinnamon. Eugenol has anti-inflammatory action through the inhibition of NF-κB, which is an important of the immune response, and it is essential to inflammatory processes to produced inflammatory cytokines and nitric oxide (NO). Besides, eugenol also increased the superoxide dismutase (SOD) catalase (CAT), glutathione peroxidase (GPx), which are necessary antioxidant enzymes that are scavenging free radicals, and also eugenol reduces inflammatory response by inhibiting the neutrophil infiltration and apoptosis through caspase-3 cleavage [27]. Cinnamon zeylanicum bark contains cinnamaldehyde, eugenol, trans cinnamon acid, hydroxyl cinnamaldehyde, and o-methoxy cinnamaldehyde [28]. Cinnamaldehyde has been reported to reduce the development of stress and serotonin-induced ulcers in mice and to reduce stomach and intestinal motility [29]. The cinnamon zeylanicum has both gastric cytoprotective and antisecretory effects at a dose of 100 mg/kg administrated orally not only increase the healing of gastric ulcers but also prevented the development of duodenal ulcers in rats [30]. Ethanol extract of Cinnamomum zeylanicum showed suppression of the intracellular release of TNF-α in murine neutrophils as well as leukocytes in pleural fluid. The extract was found to inhibit TNF-α gene expression in LPS-stimulated human PBMC at 20 μl/ml concentration. Potent anti-inflammatory activity of the cinnamon extract is suggestive of its anti-arthritic activity, which could be confirmed in various models of arthritis [31]. The phenolic content of Cinnamomum zeylanicum bark relatively high, proved its antioxidant and free radical scavenging activity in the vitro study [32]. Methanolic extract of cinnamon bark contains several antioxidants compounds that scavenged many kinds of reactive oxygen species, such as superoxide anions and hydroxyl radicals, as well as other free radicals under in vitro conditions [33]. Manuka honey is rich with flavonoids, which are polyphenolic compounds that have many pharmacological activities such as (anti-inflammatory, antioxidant, gastroprotective, and antisecretory) and prevent gastric ulcer formation. Manuka honey significantly decreased the ulcer index, completely protected the mucosa from injured agents, and preserved gastric mucosal glycoprotein. Manuka honey also increased considerably gastric mucosal level of antioxidants (SOD and GPx) and significantly decreased gastric mucosal MDA and plasma inflammatory cytokines such as TNF-α, IL-β, and IL-6 [34].

In this research, we study the effect of cinnamon on the expression of SOD-1 and TNF-α in gastric ulcer-induced by indomethacin in rats. It can be seen that the antioxidant and anti-inflammatory effects of cinnamon help to prevent the formation of gastric ulcers induced by indomethacin. The result of our research showed, administration of 30 mg/kg body weight of indomethacin on the first day (C+ 1st day) group reveals significantly decreased expression of SOD-1 (antioxidant enzyme) and significantly increased expression of TNF-α (a pro-inflammatory cytokine) compared with the control group. In the treatment groups (T1, T2, and T3) with cinnamon extract at doses (100, 200, and 400 mg/kg b.w) respectively showed significantly increased expression of SOD-1 and significantly decreased expression of TNF-α compared with control positive on the first day (C+ 1st day) group. Moreover, the indomethacin groups cause gastric erosion or ulcer formation with an increase of inflammatory cells infiltration around the gastric lesions, while the treatment groups with cinnamon extract reveal improved gastric histopathology, including the gastric erosion and inflammatory cells infiltration compared with indomethacin groups.

**SUMMARY**

In this study, it is concluded that cinnamon extract administration after gastric ulcer-induced by indomethacin increasing expression of SOD-1, decreasing expression of TNF-α, and improving the gastric histopathology and it demonstrates that administration of cinnamon extract could protect against an indomethacin-induced gastric ulcer in rats via their antioxidant and anti-inflammatory properties.
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