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The role of camel milk as a protective factor on rats infected with indomethacin-induced gastric ulcer

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Abstract

This research was conducted to evaluate the nutritional content of camel milk and the difficulties that accompany them when taken with indomethacin. The results observed that camel milk is a rich source of nutritional values and antioxidants. The biological experimental was divided into six groups. The first group was control negative, and the groups G2, G3, G4, and G5 had orally one dose of indomethacin (30 mg/kg body weight) to induce ulcers. The G2 was considerably a positive control, and the groups G3, G4, and G5 had orally 5, 10, and 15 mL/kg body weight daily camel milk. The results observed that camel milk markedly raised concentrations of enzymatic antioxidants while concurrently lowering malondialdehyde levels in comparison to the positive group. However, rats taken orally 15 mL/kg camel milk showed significantly lower serum IL-6 and tumor necrosis factor-α concentration compared to 5 and 10 mL/kg camel milk. Rats given indomethacin showed a significant decrease in cyclooxygenase (COX-2) and prostaglandin E2 (PGE2) levels and also a significant increase in cytochrome P450 reductase activity. These results were based on the measurements of cyclooxygenase activity, PGE2 concentration, and cytochrome P450 reductase activity in the gastric tissues. The results from macroscopic examination and histopathological examination of gastric ulcers in normal and treated rats groups with camel milk confirmed the above results by serum and gastric tissue. Therefore, camel milk has a potent ulcer-healing impact on gastrointestinal injury caused by indomethacin. The potential cytoprotective mechanism and antioxidant characteristics of camel milk may be responsible for its antiulcer efficacy.

Keywords: camel milk; gastric ulcer; antioxidant enzyme; gastric mucosa.

Practical Application: Camel milk has a potent ulcer-healing impact on gastrointestinal injury caused by indomethacin.

1 INTRODUCTION

Toxic compounds harm the gastrointestinal (GI) mucosa, which is thought to be the first line of defense against xenobiotics. According to Zhang et al. (2012), severe GI mucosal ulcers may cause GI bleeding or even perforation. Due in large part to their regular use of non-steroidal anti-inflammatory drugs and higher standard of life, people in the lowest income bracket are more likely to develop gastric ulcers, which is one of the leading causes of morbidity worldwide (Abubakar et al., 2018).

Ulcer is a potentially fatal illness that affects millions of individuals worldwide. According to Klein et al. (2010), it is typified by a rupture of the mucous membrane lining the alimentary canal. The fundamental pathophysiology of gastric ulcers is caused by an imbalance between cellular protective and endogenous factors (Konturek et al., 2005).

Gastric ulcers are caused by a number of factors, including alcoholism, smoking, dietary inadequacies, and frequent utilization of anti-inflammatory medicines. Coffee, spicy food, and emotional stress are all things that might make the stomach secrete more acid and aggravate an ulcer that already exists (Satyanarayana, 2006).

There is no milk that is more like human milk than camel milk, sometimes known as the "white gold of the desert." Low in sugar, cholesterol, and high in minerals, high in vitamins, and rich in protective proteins like albumin, immunoglobulins, lactoferrin, and lactoperoxidase set it apart from other ruminant milks (Kula, 2016).

Camel milk contains a high amount of mineral contents and has high concentrations of vitamins (Al-Bashan, 2011). Given that magnesium is necessary for the metabolism and absorption of vitamins B, C, and E, these vitamins can help lessen the oxidative stress brought on by hazardous agents (Traber & Stevens, 2011). Furthermore, magnesium is essential for the formation of glutathione (GSH) and guards against heavy metals, peroxides, and free radicals damaging cellular components. Magnesium has been shown more recently to greatly improve the antioxidant defense. According to Jihen et al. (2011), zinc has been shown to have a protective impact against cellular toxicity because it has a soothing influence on oxidative stress, activates the antioxidant system, and reduces lipid peroxides. Additionally, it has the ability to produce nitric oxide, which promotes the creation of mucus, prevents neutrophils from adhering to endothelial cells, and, most importantly, enhances the movement of blood to the mucous membrane lining the stomach (Al-Wabel et al., 2012).

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Because camel milk has a higher whey protein to casein ratio than other forms of milk, it is easier to digest and has a mild effect on the digestive system (Hajian et al., 2020). Thus, the aim of this research is to study camel milk's potential in the treatment of stomach ulcers.

2 MATERIALS AND METHODS

2.1 Materials

Camel milk was obtained from a local market in Saudi Arabia and it was transferred into sterile tubes and stored at -80°C.

Hajrezaie et al. (2012) stated that rats were administered 30 mg/kg body weight of the saltwater-dissolved indomethacin, which was acquired from Sigma-Aldrich.com.

In this investigation, 30 adult rats weighing between 190 and 210 g were employed. The animals were kept in typical laboratory settings in plastic cages with an aluminum top that was filled with sawdust. Before the research started, the rats were given growers necessary meals, continual tap water, and 2 weeks to get used to their new environment.

2.2 Method

2.2.1 Determination of physical–chemical and mineral content

The AOAC (2010) conducted an analysis of camel milk to determine its proximate composition, which includes moisture, crude protein, fat, ash, total solids, lactose, pH, and total carbohydrates. Furthermore, the mineral content of camel milk was determined in accordance with the AOAC (2010) technique. The minerals included zinc, iron, copper, manganese, calcium, manganese, potassium, and sodium.

2.2.2 Antioxidant activity and antioxidant content in camel milk

Total phenolic (TP) in camel milk was measured according to Qawasmeh et al. (2012) using the Folin-Ciocalteu reagent assay as gallic acid equivalents (mg GAE/L) dry weight.

According to Eghdami and Sadeghi (2010), the total flavonoids in camel milk were reported as mg QE/l (milligrams of quercetin equivalents) dry weight.

2.2.3 Total antioxidant capacity

The TAC test was carried out by measuring the quantity of hydrogen peroxide (H2O2) in camel milk sample and evaluated spectrophotometrically at 505 nm to assess the residual H_2O_2 colorimetrically (Koracevic et al., 2001).

2.3.4 DPPH radical scavenging activity assay

Using DPPH, the water-soluble extracts' radical scavenging activity was in accordance with Lim and Quah (2007). The Equation 1 is used to determine the extracts' ability to scavenge radicals:

$$\% = (1-\text{Absorbance}_{\text{sample}}/\text{Absorbance}_{\text{control}}) \times 100 \quad (1)$$

2.3.5 Ferrous ion chelating activity assay

Water-soluble extracts' FCA was determined in accordance with Chan et al.'s (2007) instructions. The extracts' FCA was computed as follows (Equation 2):

$$\text{FCA\% is calculated as} = (1-\text{Absorbance}_{\text{sample}}/\text{Absorbance}_{\text{control}})\times 100 \quad (2)$$

2.3.6 Ferric-reducing capacity assay

Oyaizu (1986) assessed ferric-reducing capacity of water-soluble extracts. The values of reducing capacity were presented in milligrams of gallic acid equivalents (GAE mg/mL).

2.3.7 Ulcer induction

To ensure an empty stomach, the rats in groups G2–G5 were starved for 48 h with unlimited access to water. After that, the animals in groups G2, G3, G4, and G5 received a single dose of indomethacin (30 mg/kg body weight) orally via gastric gavage needles, and they were left to wait for the onset of ulcers for a full day (Bhattacharya et al., 2007). After that, for 14 days, the camel milk therapy was administered as directed.

2.3.8 Experimental groups

The rats were re-divided into five groups and fed on a basal diet for 14 days as well as treated as follows:

- Group 1 (G1) Negative control: Placed on distilled water;
- Group 2 (G2) Positive control: Indomethacin-induced ulcer untreated;
- Group 3 (G3) Indomethacin-induced ulcer treated orally with 5 mL/kg/day of camel milk (every rat equal 200 g taken orally/day 1 ml camel milk);
- Group 4 (G4) Indomethacin-induced ulcer treated orally with 10 mL/kg/day of camel milk (every rat equal 200 g taken orally/day 2 mL camel milk);
- Group 5 (G5) Indomethacin-induced ulcer treated orally with 15 mg/kg/day of camel milk (every rat equal 200 g taken orally/day 3 mL camel milk).

2.3.9 Gastric mucosal lesion biomarkers

After 14 days, the animals were sacrificed and the stomachs were opened and washed with 0.9% NaCl as well as examined for macroscopic lesions in the glandular parts (Ohta et al., 1997).

2.3.10 Determination of gastric oxidative stress biomarkers

Yoshioka et al. (1979) used a calorimeter to determine malondialdehyde (MDA). Additionally, the approach with Sairam et al. (2003) was used to assess the activity of superoxide dismutase (SOD), whereas Habig et al. (1974) measured the non-enzyme GSH. Catalase (CAT) activity was measured according to Abubakar et al. (2018).

2.3.11 Determination of serum pro-inflammatory cytokines

Serum separation was achieved by centrifuging the blood samples. According to Millena et al. (2004), the serum levels of tumor necrosis factor-α (TNF-α) were measured using an EpiQuikTM kit (OP-0002, EpiGentek, NY, USA). IL-6 (interleukin) was quantified using kits. Every operation was carried out in accordance with the description by Althaiban (2018).

2.3.12 Histological examination

The animals were slaughtered after 14 days, and the more carefully opened stomachs were removed, stomach mucosa and lesions were assessed macroscopically, and the tissue was evaluated histopathologically.

2.3.13 Gastric mucosa determination

The criteria for cyclooxygenase gastric (COX-2) cytochromes, prostaglandin E2 (PGE2), and cytochrome P450 reductase (were used to determine the gastric mucosa according to Hamberg and Samuelsson (1973), Hemler and Lands (1976), and McLean and Day (1974).

2.3.14 Macroscopic evaluation

In accordance with Ohta et al. (1997), the macroscopic lesions in the glandular sections were investigated. In accordance with Yam et al. (2009), the glandular ulcer's severity was evaluated semi-quantitatively using the following scale: normal mucosa is denoted by 0, hyperemic mucosa by up to two patches, and a loss of mucosal folding by three small patches or more.

2.3.15 Histopathological examination

At the conclusion of the trial, gastric specimens were taken from each group and preserved in a 10% neutral buffered formalin solution for histology. The tissue samples underwent the following procedures: they were sectioned at a thickness of 5 µm, cleaned in xylene, embedded in paraffin wax, and dehydrated in ethanol at increasing concentrations. Hematoxylin and eosin (H&E) staining were applied to prepared slide slices, which were then observed under a light digital microscope (Olympus XC30, Tokyo, Japan) (Trajković et al., 2007). According to Muller-Quernheim (1998), the histopathological changes of the stomach were evaluated semi-quantitatively in five randomly selected high microscopic magnification fields (20x) per group to evaluate the lesions: loss of epithelium, necrosis, edema, and inflammation. Gastric tissue norm = 0. A score of +1 was assigned to gastric tissue with modest histological damage. Moderately altered individuals are number 2, whereas severely altered individuals are number 3.

2.3.16 Statistical analysis

The statistical study includes a one-way analysis of variance and an LSD test for multiple comparisons, and it was carried out using the Statistical Product and Service Solutions (SPSS) software (version 17). SAS (2004) stated that all data were given as mean ± SE and that statistical significance may be predicted if $p \leq 0.05$.

3 RESULTS AND DISCUSSION

3.1 Nutritional value for camel milk

Chemical compounds present in camel milk are moisture, crude protein, fat, ash, total solids, and total carbohydrates, as well as mineral contents such as zinc, iron, calcium, manganese, potassium, and sodium (Table 1). The most significant component of camel milk, according to the research, is its 85.12% water content. In contrast to other animals, camels lose more water when they become dehydrated. The water content is 86% in milk when it is readily available, but it increases to 91% when water is restricted. In places where water is scarce, this can be used as a supply of water for humans and dehydrated calves (Sisay & Awoke, 2015). The dehydrated camel's increased ADH secretion, decreased fat content, and the kind of feed it consumes are the causes of increased water content in milk (FAO, 2013). Furthermore, research indicated that camel milk had a total solids concentration of 11.8%. These outcomes matched the values reported by Abbas et al. (2013).

Protein in camel milk is 3.94%. This finding might be explained by the fact that camel milk proteins are a diverse collection of substances with varying compositions and characteristics (Gizachew et al., 2014). Milk from dromedary camels has 3–3.90% protein. In addition to a comparatively larger concentration of immunological proteins, it comprises two major classes of proteins: caseins and whey (Gul et al., 2015).

The level of fat in camel milk was found to be 4.52%. This result was confirmed by Konuspayeva et al. (2009), who discovered that fat content ranges from 2.9 to 5.4% in camel milk. Humans may, therefore, digest milk from camels more easily (D'Urso et al., 2008). Camel milk had higher long-chain fatty acids (96.4 %) in its lipid component compared to 85.3% in bovine milk (Abbas et al., 2013). Additionally, the amount of lactose in camel milk was 4.21%, which was supported by the findings of Kumar et al. (2016), who discovered that the lactose level in camel milk is consistent and ranges from 3.5 to 4.5%.

The macro-composition of camel milk, according to Behrouz et al. (2022), includes water, fat, protein, percent milk solids, ash, and lactose, with 86.3–88.5, 2.9–5.5, 2.5–4.5, 2.9–5.8, 0.35–0.95, and 2.9–5.8%, respectively. Throughout the experiment, camel milk's pH was found to be 6.6. This observation is

Table 1. Chemical composition (on dry weight) and minerals content (mg/100 g) of chemical milk*.

Chemical composition	Camel milk %	Minerals content	Camel milk mg/100 g
Moisture	85.12 ± 3.25	Zinc	0.49 ± 0.03
Protein	3.94 ± 0.13	Iron	0.38 ± 0.01
Fat	4.52 ± 0.15	Copper	0.11 ± 0.01
Ash	0.81 ± 0.07	Manganese	0.05 ± 0.001
Total carbohydrates	1.63 ± 0.08	Calcium	112.17 ± 7.29
Total solids	11.8 ± 1.68	Magnesium	11.85 ± 1.36
Lactose	4.21 ± 0.24	Potassium	160.16 ± 10.56
pH	6.6 ± 0.13	Sodium	55.11 ± 3.18

*Mean values (± standard deviation) within the same column.

harmonious with Khaskheli et al. (2005), who found that camel milk has a pH ranging between 6.0 and 6.7.

Lactose sugar is the main carbohydrate, accounting for 1.63% of the milk from camels, and its percentage varies from 3.3 to 5.80%. Widespread variation in lactose concentrations may be attributed in part to the type of plants that camels in desert regions consume (Abbas et al., 2013).

Zinc is an essential component of the immune system, a co-factor in numerous enzymes, and a protector against cell damage. According to Shamsia (2009), the average zinc level in camel milk is 0.49 mg/100 mL, which is greater than that in cow and human milk, which are 0.38 and 0.165 mg/100 mL, respectively.

However, Aludatt et al. (2010) stated that iron is an essential part of hemoglobin, which is needed for the brain, enzyme systems, red blood cell creation and function, oxygen delivery, and red blood cell formation. The study's iron concentration was 0.38 mg/100 mL, which is in agreement with that of Shamsia (2009).

The stated iron content in breast milk was lower than that in camel milk. Breast milk's iron level ranges from 0.013 to 0.046 mg/100 mL, according to Cai et al. (2015). Given that camel milk has a higher iron content than breast milk, it may be a preferable alternative to human milk in situations when iron supplementation is necessary. Those who suffer from anemia or malnourishment may find it helpful (Aludatt et al., 2010).

According to WHO and FAO (1996), copper has a catalytic role in the development of connective tissue and red blood cells, as well as supports central nervous system function. According to our data, the average Cu level in camel milk was 0.11 mg/100 g, which was greater than in cow milk (Shamsia, 2009; Soliman, 2005).

Additionally, camel milk has the highest concentrations of important minerals, including sodium, potassium, calcium, magnesium, and manganese, at 0.05, 112.17, 11.85, 160.16, and 55.11 mg/100 g, respectively. Numerous minerals are abundant in camel milk. It has antiulcer property since it is high in magnesium and zinc (Kula, 2016).

3.2 Antioxidant activity and antioxidant content in camel milk

Results from Table 2 show that antioxidant contents such as TAC, (mmol/L), TP (mg GAE/L), and flavonoids (mg QE/L) in camel milk.

Table 2. Antioxidant activity and antioxidant content in camel milk*.

Antioxidant activity	Camel milk	Antioxidant content	Camel milk
DPPH radical scavenging activity (%)	84.8 ± 0.90	Total antioxidant capacity (TAC) (mmol/l)	2.27 ± 0.13
Ferrous ion chelating activity (%)	57.6 ± 1.22	Total phenolic content (mg GAE/L)	32.91 ± 0.19
Ferric-reducing capacity (mg GAE/mL)	5.63 ± 0.02	Total flavonoids (mg QE/L)	21.25 ± 0.07

*Mean values (± standard deviation) within the same column.

The results point out that the TAC was 2.27 mmol/L. This finding, which was supported by Kaur and Kapoor (2001), suggested measuring TAC, an important metric for confirming the nutritional value of food. Turhan et al. (2011) discovered that camel milk has more TAC than human and cow milk. TAC data (3.6 ± 0.14 mmol/L) acquired in this investigation was higher than the TAC data for human (1.8 mmol/L) and bovine (2.24 mmol/L) milk.

Additionally, the TP content and flavonoid component in camel milk were elevated at 32.91 mg GAE/L and 21.25 mg QE/L, respectively. These findings are supported by Bouhaddaoui et al. (2019) illustration, which shows that camel and goat milk had high amounts of phenolic content of 35.45 mg GAE/L and 39.2 mg GAE/g, respectively. Milk from cows only has 28 mg GAE/L. Furthermore, camel milk is high in flavonoids, with 29.05 mg EQ/L, compared to 25.3 mg and 31.3 mg in cow and goat milk, respectively. The kind and makeup of the plants ingested may also play a role in the flavonoid content of dromedary milk.

The same table illustrates the results from DPPH radical scavenging activity (%), FAC (%), and ferric-reducing capacity (mg GAE/mL) in camel milk with 84.8%, 57.6%, and 5.63 mg GAE/mL, respectively. These outcomes were in agreement with Sultana et al. (2007), who found that camel milk contains a high amount of natural antioxidants, which are important because they may act as free radical scavengers or inhibitors and may be responsible for the higher activity of DPPH. These compounds may even function as primary antioxidants.

Dairy products' antioxidant activity is important for the goods' shelf life and quality as well as for defense against the body's overproduction of oxygen-free radicals (Alenisan et al., 2017). Research has indicated a negative correlation between the occurrence of specific diseases and the use of foods high in natural antioxidants (Alenisan et al., 2017). Through a variety of methods, dietary antioxidants are substances that can scavenge free radicals and stop harmful influences (Stobiecka et al., 2022).

Excellent exogenous antioxidant supplements like camel milk can be used to reduce the oxidative stress linked to a variety of illnesses, including cancer and hepatitis. The main components of camel milk are caseins, LAB, bioactive peptides, and whey proteins, particularly lactoferrin (Habib et al., 2013). All of these components have antioxidant activity.

3.3 Biological experimental

Today, peptic ulcers afflict people everywhere, even in remote areas of the world. It is widely acknowledged that an imbalance between aggressive forces and endogenous defense mechanisms' ability to maintain mucosal integrity leads to peptic ulcers. Indomethacin is known to induce stomach ulcers by blocking prostaglandins, which are cytoprotective to the gastric mucosa (Morsy & El-Moselhy, 2013). This is particularly true since it suppresses the arachidonic acid metabolism's COX pathway, which causes an overabundance of leukotrienes and other 5-lipoxygenase pathway products to be produced.

3.4 Measurement of gastric oxidative stress biomarkers

Table 3 reports the results of a study that measured lipid peroxidation as measured by MDA, as well as the activity of antioxidant enzymes such as GSH reduced, SOD activity, and CAT in various groups of rats given oral indomethacin to induce gastric ulcers and treated with varying amounts of camel milk.

The results revealed that the SOD, GSH, and CAT levels significantly increased gradually in rat groups treated with camel milk compared with the ulcerated positive group. While the MDA level was considerably lower for all camel milk treated groups. Furthermore, after consuming 15 mL/kg/rat of camel milk daily after 14 days, the levels of GSH, SOD, CAT, and MDA in all treatment groups attained values that were marginally comparable to those of the normal group: 88.95 mmol/L, 70.16 µmol/L, 8.64 µ/mg, and 6.48 mmol/L, respectively. Furthermore, a decrease in hunger, disruption of the secretions of stomach enzymes, and changes in the pH of the gastric secretion could all be contributing factors to the decline in control positive. These outcomes agree with the conclusions drawn by Haithem et al. (2014). The pathophysiology and progression of indomethacin-induced stomach damage have been linked to oxidative stress (Orsi et al., 2014). According to Halici et al. (2005), non-steroidal anti-inflammatory medicines (NSAIDs) like indomethacin have been shown to reduce the antioxidant enzymes (SOD, CAT, and GSH) in the duodenum and stomach, which can lead to gastric ulcers. Free and oxygen-derived radicals may be produced status brought on by the decline in antioxidant enzymes' activity (Ajiboye et al., 2010). Eating camel milk may increase the activity of these antioxidant enzymes, which could be a significant defense against hydroxyl, superoxide, and peroxide radicals (Hu et al., 2017; Kaur & Sen, 2017).

According to Monari et al. (2009), a decrease in CAT activity is typically seen in gastric cancer and stomach infected with *Helicobacter pylori*, while an increase in SOD activity has been related to ulcer healing. In multiple researches, camel milk's (CM) exogenous antioxidant potential was established through the reduction of oxidative stress (Krishnankutty et al., 2018). According to Khan et al. (2021), camel milk is thought to have higher antioxidant activity because it contains 6.7 times more vitamin C than fresh cow milk, along with other antioxidant-rich ingredients.

3.5 Pro-inflammatory cytokines such as TNF-α and IL-6

Administration of rats with indomethacin (control positive) significantly increased both serum IL-6 and TNF-α (26.38 and 3.18 ng/mL) compared to the control negative rats, which were 13.76 and 1.67 ng/mL, respectively. The pretreatment of rats with camel milk at 5, 10, and 15 mL/kg significantly gradually reduced serum IL-6 and TNF-α concentration compared to the indomethacin-positive group. However, the rats pretreated with 15 mL/kg camel milk showed significantly lower serum IL-6 and TNF-α concentration compared to 5 and 10 mL/kg camel milk (Table 4).

According to Sugimoto et al. (2007), cytokines are a diverse class of polypeptides with a variety of functions, including modifying, inducing, and regulating immunological and inflammatory responses. Reactive oxygen species might eventually cause less tissue damage if IL-6 and TNF-α were inhibited (Kwiecien et al., 2002). In comparison to the control rats, the current study showed a considerable rise in both cytokines: TNF-α and IL-6.

One of the most significant immuno-modulatory cytokines is TNF-α, which elevates the inflammatory verbal by the production of free radicals, arachidonic acid metabolites, proteases, and some cytokines (Behrouz et al., 2022). Throughout inflammation, migrating macrophages allow TNF-α, an important pro-inflammatory cytokine (Rozza et al., 2014). It prevents gastric microcirculation everywhere in ulcerated mucosa, supports neutrophil infiltration in gastric inflamed areas (Aziz et al., 2019), and postpones the healing of stomach ulcers (Hasgul et al., 2014).

The findings of this study suggest that camel milk has a gastroprotective activity that is linked to an antiulcerogenic impact. It also dramatically decreases the amount of gastric ulcers caused by indomethacin and shows an antiulcer effect in all three models when used in the gastroprotective technique.

3.6 Influence of camel milk on gastric tissues treated with indomethacin

According to Table 5, when rats were given indomethacin, their levels of gastric COX-2, PGE2, and cytochrome P 450 reductase activity (Cyto P450) significantly decreased than the

Table 4. Serum tumor necrosis factor-alpha (TNF-α) and IL-6.

Groups	TNF- alpha (ng/mL)	IL-6 (ng/mL)
Control negative	1.67 ± 0.54 [d]	13.76 ± 0.76 [c]
Control positive	3. 18 ± 0.38 [a]	26.38 ± 1.25 [a]
Group (3)	2.66 ± 0.390 [b]	22.39 ± 0.94 [b]
Group (4)	2.13 ± 0.32 [c]	18.61 ± 1.28[ab]
Group (5)	1.60 ± 0.46 [d]	14.12 ± 1.48 [a]

Values are mean and SD (n = 6) within the same with the letter differ significantly at $p \leq 0.5$ levels.

Table 3. Influence of camel milk on gastric oxidative stress.

Groups	GSH (mmol/L)	SOD (µmol/L)	MDA (mmol/L)	CAT (µ/mg)
Control negative	95.68 ± 7.25[a]	75.35 ± 6.26[a]	5.09 ± 0.43[d]	9.09 ± 1.32[a]
Control positive	34.08 ± 2.04[e]	19.58 ± 1.22[e]	12.20 ± 1.53[a]	2.50 ± 0.01[d]
Group (3)	46.64 ± 3.12[d]	27.61 ± 2.27[d]	10.58 ± 1.24[b]	4.67 ± 0.11[c]
Group (4)	63.63 ± 3.59[c]	37.31 ± 3.86[c]	8.72 ± 0.76[bc]	6.49 ± 0.21[bc]
Group (5)	88.59 ± 5.28[b]	70.16 ± 6.51[b]	6.48 ± 1.08[c]	8.64 ± 0.35[b]

*Values are mean and SD (n = 6) within the same with the letter differ significantly at $p \leq 0.5$ levels.

normal control group. These outcomes agree with those of an earlier investigation (Whittle, 2003). A specific COX-2 inhibitor postpones the suppression of the mucosa, including its defense and repair mechanisms as well as the ulcerative stomach mucosa brought on by COX-2. It is at best found in stomach mesenchymal cells, according to Miura et al. (2004). This suggests that COX-2 is expressed in mesenchymal cells around the ulcer's edge and plays a critical role in the process of ulcer repair. Comparing the camel milk treatment to the indomethacin-treated rats showed a substantial inverse effect on all participants. These results are consistent with those from earlier research (Borrelli & Izzo, 2000). It was shown that flavonoids protect against damage to the gastric mucosa by raising prostaglandin mucosa levels and preventing histidine decarboxylase from releasing histamine from mast cells. By reducing COX-2 activity, camel milk appears to have anti-inflammatory property (Aneta et al., 2013). The phenolic content of camel milk is abundant and is known to have antioxidant property (Godevac et al., 2012).

Table 5. Effect of camel milk on gastric tissues treated with Indomethacin*.

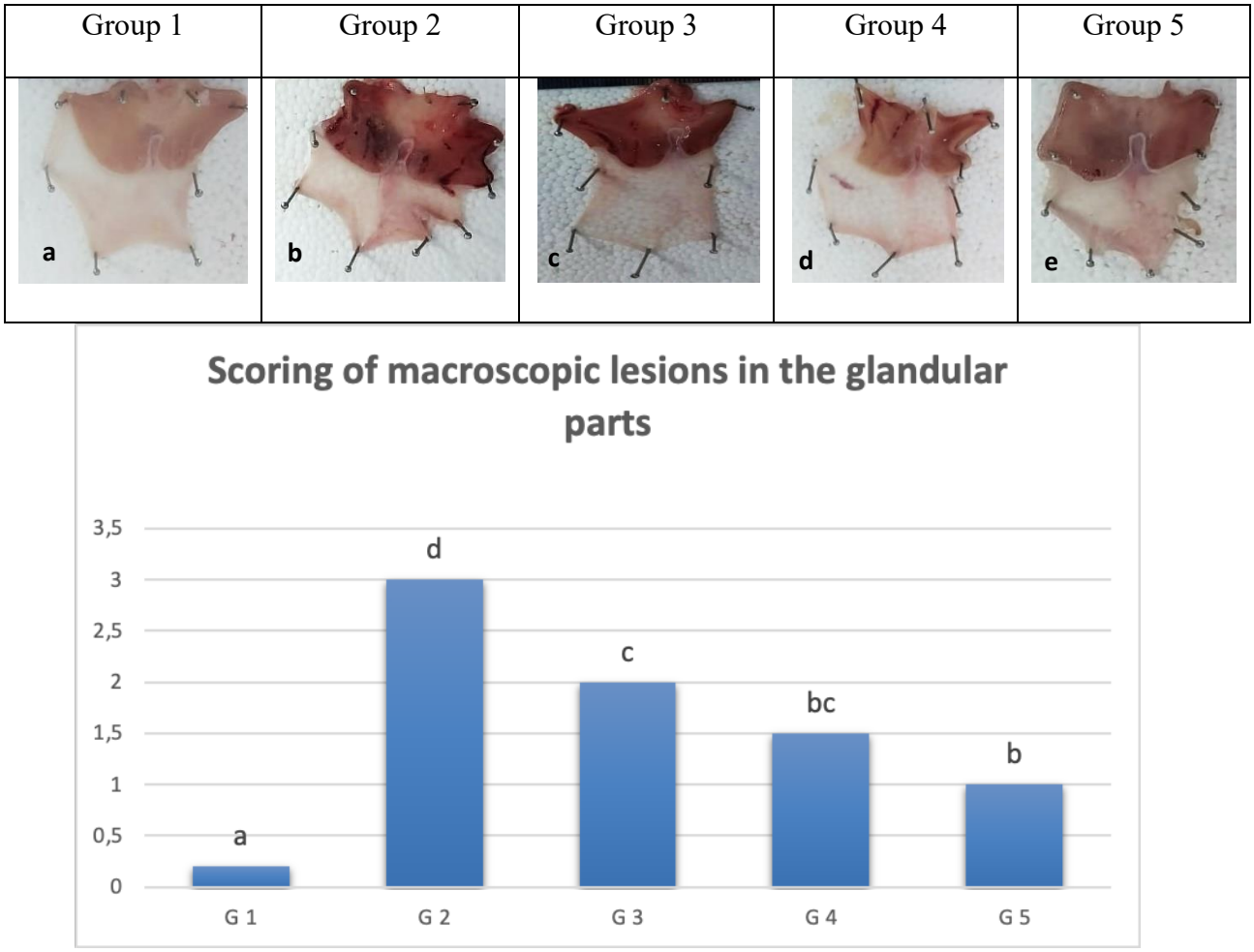
Groups	Cox-2 ng/mg	PGE2 pg/mg	Cyto P450 ng/mg
Control negative	4.43 ± 0.91^{a}	384.25 ± 25.14^{a}	9.45 ± 0.98^{d}
Control positive	2.23 ± 0.51^{d}	147.77 ± 10.14^{d}	19.23 ± 2.11^{a}
Group (3)	2.99 ± 0.42^{c}	223.36 ± 15.48^{c}	15.97 ± 1.75^{b}
Group (4)	3.72 ± 0.31^{b}	300.47 ± 17.38^{b}	12.75 ± 1.12^{c}
Group (5)	4.33 ± 0.62^{a}	378.29 ± 14.26^{a}	10.95 ± 9.78^{d}

*Values are mean and SD ($n = 6$) within the same with the letter differ significantly at $p \leq 0.5$ levels.

The investigation data, as shown in Tables 1 and 2, indicated that the main phytoconstituents in camel milk showed strong antioxidant activity and were in charge of giving rats the gastroprotective effects against indomethacin. Indomethacin rats administered camel milk showed a considerable improvement in all evaluated parameters. Rats in treatment groups had camel milk volumes of 5 mL, 10 mL, and 15 mL that were comparable to normal levels for each and every parameter. These results can be attributed to the antioxidant property of camel milk, which repair and restore the gastric ulcers of damaged rats.

3.7 Macroscopic examination of gastric ulcers

The macroscopic pictures of stomachs from all experimental groups observed that the first Control group (Figure 1A) was a normal stomach. The second group of rats,



*Values are mean and SD ($n = 6$) within the same with the letter differ significantly at $p \leq 0.5$ levels.

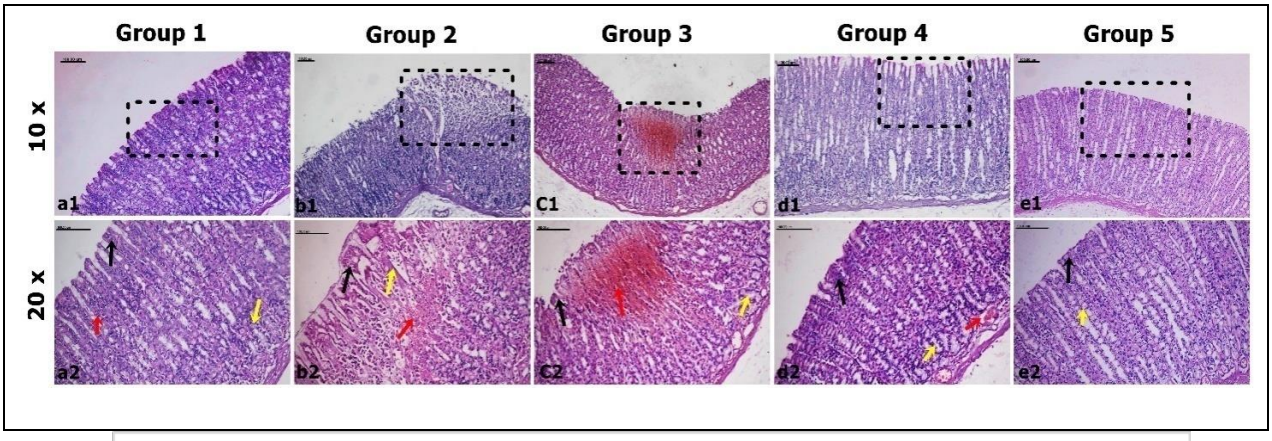
Figure 1. Macroscopic pictures of stomach from all experimental groups. (A) Control group, (B) indomethacin, (C) indomethacin + 1 mL camel milk/day, (D) indomethacin + 2 mL camel milk/day, and (E) indomethacin + 3 mL camel milk/day*.

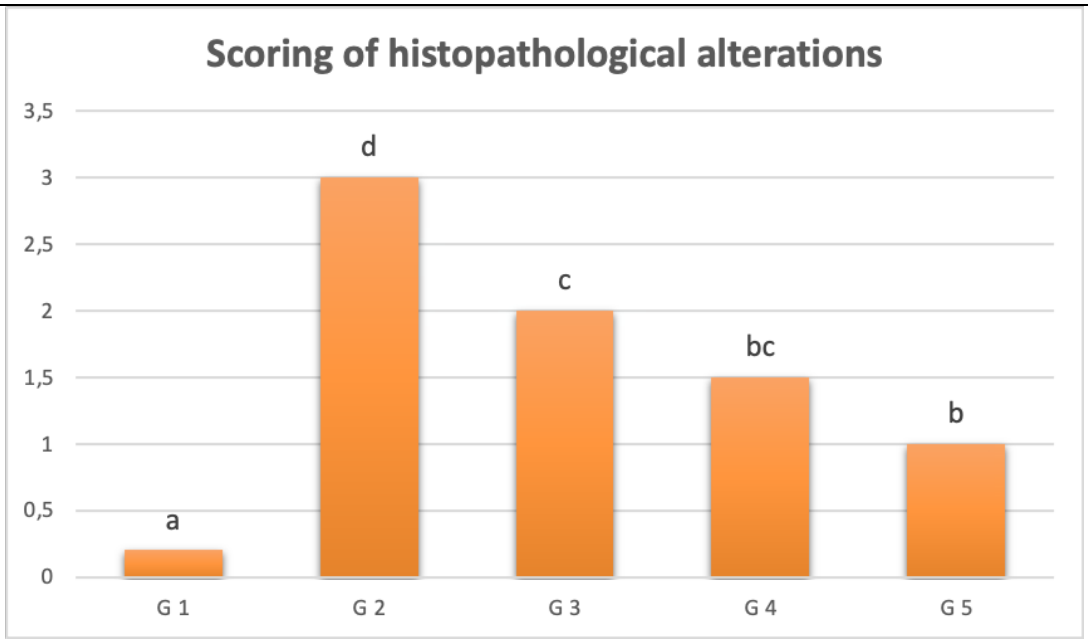
which were administered indomethacin, exhibited macroscopic signs of gastric tissue damage, including discoloration, several severe hemorrhagic ulcerative lesions, which ranged from deep hyperemic regions to hemorrhagic elongated lines, and edema (Figure 1B). The delivery of 5 mL/kg of camel milk to group 3 marginally attenuates macroscopic changes, with certain fields exhibiting hyperemia and mucosal loss (Figure 1C). Furthermore, a few macroscopic alterations were visible, such as intermittent localized hyperemic pinpoint lesions in group 4 (10 mL/kg of camel milk) (Figure 1D). In addition, compared to the untreated control group (Figure 1A), rats in group 5 that received 15 mL/kg of camel milk were able to reverse the moderate hyperemia caused by indomethacin (Figure 1E).

Consuming camel milk promotes the growth of a greater quantity of *Bifidobacterium*, *Akkermansia*, and *Allobaculum*, which enhances the gut microbiota. Wang et al. (2018) found that camel milk may have a high amount of *Allobaculum*, which could have a good impact on the organism's physiological processes. Short-chain fatty acids produced by this genus reduce inflammation, avoid obesity, and enhance colon health. The probiotic *Akkermansia* is well known for its positive benefits on inflammation, metabolic diseases, obesity, and diabetes because it breaks down mucins (Wang et al., 2018).

3.8 Histopathological examination of gastric ulcers

The basal mucosa of the control group stained with H&E underwent normal histological examination, revealing an intact surface epithelium composed of simple columnar mucin-secreting cells extending into the lamina propria to produce gastric pits (Figure 2A1). Fundic glands span the entire thickness of the lamina propria and are oriented perpendicular to the surface (Figure 2A2).





*Values are mean and SD ($n = 6$) within the same with the letter differ significantly at $p \leq 0.5$ levels.

Figure 2. Photomicrographs of gastric mucosa and submucosa layers showing (a1) normal fundic mucosa (black square), (a2) gastric pits (red arrow) and gastric gland (yellow arrow). (b1) Erosions and ulcerative lesions (black square), (b2) edema (yellow arrow) and hemorrhage mixed with inflammatory cells (red arrow). (C1a, b) Hemorrhagic gastritis (black square) and desquamation of lining epithelium (black arrow). (d1.2) Pyknotic cells (black arrow) and congested blood vessels (red arrow). (e1,2) Apparently healthy mucosa and submucosa layers.

In contrast, group 2 (30 mg/kg indomethacin) displayed more severe pathological changes to the stomach tissue, such as noticeable erosions and ulcerative lesions of the tunica mucosa, which were characterized by fundic mucosa sloughing, desquamation, and loss of the mucosal layer's basement membrane (Figure 2B1). Furthermore, there is a deterioration of the stomach gland and a light pink exudate (edema) combined with inflammatory cells infiltrating the submucosal layer (Figure 2B2).

Hemorrhagic gastritis, inflammatory cell infiltration, and desquamation of the gastric mucosa were observed in group 3 (30 mg/kg Indomethacin+5 mL/kg camel milk/day), which demonstrated a modest amelioration of the fundic mucosa (Figure 2C1,2). However, group 4 (30 mg/kg Indomethacin+10 mL/kg camel milk/day) maintained the histological architecture of the stomach tissue, with only a few pathological changes—such as blood vessel congestion and partial cell pyknosis—observed in sporadic rats (Figure 2D1,2). Additionally, group 5 (30 mg/kg indomethacin + 15 mL/kg camel milk/day) exhibited a more notable improvement in the histological structure of the stomach layers, with only minor alterations noted, such as vacuolar degeneration of the epithelium lining the tunica mucosa. Additionally, there are no erosions or ulcers (Figure 2E1,2).

Prostaglandins are essential for the stomach's defense because they promote the secretion of bicarbonate and mucus, preserve mucosal blood flow, and control the turnover and repair of mucosal cells. Consequently, NSAIDs that inhibit prostaglandin synthesis make mucosal damage and gastroduodenal ulcers more likely. According to El-Ashmawy et al. (2016), a number of studies have shown that reduced aggressive factors, including acid and pepsin secretion and enhanced mucosal resilience, are the reasons for prostaglandins' ability to protect the gastroduodenum.

The histological investigation conducted in this study revealed that the administration of indomethacin resulted in stomach architecture destruction and gastric lesions with symptoms of moderate to severe inflammation, as well as evident damage to the mucosa. When camel milk was administered, the stomach's mucosa was protected and healed, as evidenced by the microscopic examination's clear definition of the mucosa and the decreased presence of inflammation and mucosal damage. The results of this investigation demonstrated that camel milk exhibited antiulcer properties and provided a noteworthy safeguard against stomach ulcers caused by indomethacin. These findings are consistent with earlier research on camel milk's gastroprotective and antiulcerogenic properties (Abubakar et al., 2018).

4 CONCLUSION

Camel milk demonstrated a potent healing effect on ulcers and stomach injuries caused by indomethacin. The cytoprotective and reactive oxygen species scavenger properties of camel milk most likely played a role. Therefore, camel milk is used in the treatment and preventative measure for stomach ulcers as well as acts as active ingredients with antioxidant property that gives it its antiulcer properties.

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