Potential effects of *Curcumin, Thyme,* and *Chamomile* Oils against Indomethacin-induced Gastric ulcer in male Wister Albino rats

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Abstract

Indomethacin (IND) is a non-steroidal anti-inflammatory drug (NSAID) used widely in the pharmaceutical industry. Although it was used as an anti-inflammatory, gastrointestinal bleeding and ulceration were reported as the main untoward effects of IND. Essential oils are prominent worldwide in traditional and folk medicine due to their healing properties and therapeutic effects. This study was carried out to investigate the potential protective effect of using some essential oils, such as Curcumin, Thyme, and Chamomile, against ulcer induced by indomethacin. Thirty-five male albino rats were classified into a standard control group and five IND-induced gastric ulcer groups, divided into non-treated control (+ve) and treated groups with Curcumin oil, Thyme oil, and Chamomile oil groups for one-month. The results revealed that the treatment with these oils could protect from IND-induced gastric ulceration. The mechanism of its gastro-protective activity may be attributed to a significant reduction in serum interleukin 6 (IL6), tumor necrosis factor-alpha (TNF-α), malondialdehyde (MDA) and High-Density Lipoprotein (HDL-C) along with significant elevation in serum total antioxidant capacity (TAC), reduced glutathione (GSH) and hematological parameters compared with ulcerated control (+ve) group. The histopathological examination confirms these acquired results.
Conclusion: The protection provided with the treatment of Curcumin, Thyme, and Chamomile oils possesses anti-ulcer potential due to their antioxidant and anti-inflammatory properties.
Keywords: Indomethacin, Gastric ulcer, Curcumin, Thyme, Chamomile, Anti-inflammatory.

التأثيرات المحتملة لزيوت الكركمين والزعتر والبابونج ضد قرحة المعدة الناجمة عن الإندوميثاسين في ذكور فئران ويستر ألبينو

مستخلص البحث:

الإندوميثاسين هو دواء مضاد للإلتهابات غير الإستيرويدية يستخدم على نطاق واسع في صناعة الأدوية. على الرغم من أنه تم إستخدامه كمضاد للإلتهابات ، فقد تم الإبلاغ عن نزيف فى الأمعاء وتقرحها كآثار رئيسية غير مرغوب فيها للإندوميثاسين. الزيوت الأساسية بارزة في جميع أنحاء العالم في الطب التقليدي والشعبي بسبب خصائصها العلاجية وآثارها العلاجية. أجريت هذه الدراسة للتحقيق في التأثير الوقائي المحتمل لإستخدام بعض الزيوت الأساسية ، مثل الكركمين والزعتر والبابونج ، ضد القرحة التي يسببها الإندوميثاسين. تم تقسيم خمسة وثلاثين من ذكور الفئران البيضاء إلى مجموعة قياسية (سالبة) ، وخمس مجموعات مصابة بقرحة المعدة التي يسببها الإندوميثاسين ، مقسمة إلى مجموعة قياسية غير معالجة (موجبة) ومجموعات معالجة بزيت الكركمين وزيت الزعتر وزيت البابونج لمدة شهر. وكشفت النتائج أن العلاج بهذه الزيوت يمكن أن يحمي من تقرح المعدة الناجم عن الإندوميثاسين. يمكن أن تعزى آلية نشاطه الوقائي إلى انخفاض كبير في الانترليوكين ٦ و عامل نخر الورم ألفا (TNF-α)، والمالوندايالدهيد(MDA)، والبروتين الدهني عالي الكثافة (HDL-C) جنبا إلى جنب مع ارتفاع كبير في إجمالي قدرة مضادات الأكسدة فى السيرم (TAC)، وانخفاض الجلوتاثيون (GSH) مقارنة بمجموعة التحكم المتقرحة (الموجبة). يؤكد الفحص النسيجي المرضي هذه النتائج المكتسبة. الخلاصة: الحماية المقدمة مع علاج زيوت الكركمين والزعتر والبابونج تمتلك إمكانات مضادة للقرحة بسبب خصائصها المضادة للأكسدة والمضادة للالتهابات.

الكلمات المفتاحية: الإندوميثاسين ، قرحة المعدة ، الكركمين ، الزعتر ، البابونج ، مضاد للالتهابات.

Introduction

Gastric ulcer is known as holes in stomach mucosa [1]. Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the causes of stomach damage, including indomethacin (IND)[2,3,4]. Medical centers have used these drugs worldwide for their ability to reduce inflammation despite many side effects, such as gastrointestinal ulcers [1]. (NSAIDs) have been found to impact several aspects of epithelial mucus secretion, mucosal blood flow, epithelial cell proliferation, bicarbonate secretion, and mucosal resistance to damage. It is worth noting that the presence of stomach acid is considered a significant contributing factor to mucosal injury [5].

Treatment of gastric ulcer depends on two main methods: declination of gastric acid production and supporting the protection of gastric mucosa [6]. Essential oils find application in a diverse range of pharmaceutical, biotechnological, and industrial contexts. They are included in several food products as flavoring agents and preservatives, serving as food additives. [7]. Curcumin (*Curcuma longa*) tremendously ameliorates inflammation and cell death, protecting the tissue from damage [8]. Curcumin oil is considered an esophagoprotective by regulating mitochondrial function by keeping the MnSOD expression and efficiency [3]. The side effects of many anti-inflammatory drugs can be prevented by using Curcumin due to its potential gastro-protection effect [9].

Thyme (Thymus vulgaris)-phenols are thymol (40%) and carvacrol (15%) [10]. Thyme oil comprises 25 bioactive compounds, such as carvacrol (56.8%), p-cymene (12.8%), γ-terpinene (11.17%), and thymol (3.99%)[11]. Thymol has been observed to exhibit a diverse array of pharmacological actions, including anti-spasmodic, antioxidant, antimicrobial, anti-cancer, anti-viral, anti-inflammatory, and growth promoter properties [12]. There are many medicinal plants, such as Chamomile (*Matricaria chamomilla L.*), which comprise Amino acid polysaccharides, fatty acids, essential oils, minerals, elements, flavonoids, and other phenolic compounds which are the primary components of *Chamomile* [13]; [14]. *Chamomile* possesses anti-spasmodic and anti-inflammatory effects, which have been observed to enhance gastrointestinal motility issues potentially. [15]. The phytochemical analysis of Chamomile revealed the existence of many compounds, including quercetin, patuletin, apigenin, apigenin-7-O-glucoside, luteolin, luteolin-7-O-glucoside, caffeic acid, chlorogenic acid, and bisabolol. [16]. This study was designed to evaluate the potential effects of *Curcumin, Thyme,* and *Chamomile* oils against indomethacin-induced gastric ulcer in male rats.

MATERIALS AND METHODS
Materials:

Thirty-five male albino rats were obtained from the Faculty of Medicine Ain Shams Research Institute animal facility (MASRI- animal facility). The average weight was 170 ±10gm.

Indomethacin capsules were purchased from a national company for the pharmaceutical and chemical industries. *Curcuma* oil (*Curcuma longa*), *Thymus* oil (*Thymus* vulgaris), and *Chamomile* oil (*Matricaria recutita*) were obtained through the Agricultural Research Center, Giza, Egypt.

Methods:

Biological study: The basal diet was administered in accordance with the established AIN-93 protocol [17]. The rats were provided with a basal diet for five days before commencing the experiment in order to facilitate adaption. Then, the rats were divided into five main groups (seven rats each). The first group was the control negative and fed on basal diet only; the second group was the control positive and fed on basal diet; groups from three to five were fed on basal diet and administered orally daily with 1ml curcumin oil, 1ml thyme oil, and 1ml chamomile oil respectively for one-month. Before the end of the experiment, six days, the groups from two to five were administered orally of freshly prepared indomethacin solution (30mg/kg body weight/ rats) to induce gastric ulcer.

The weekly body weight gain, daily food intake, and feed efficiency ratio (FER) were calculated using the method of [18]. Rats were slaughtered following an overnight fast under ether anesthesia at the end of the one-month experiment. Blood samples were drawn from the hepatic portal vein, a small portion was placed in a heparinized tube, and the remaining was allowed to clot at room temperature for 15 minutes before being centrifuged at 3000 rpm for 20 minutes. The serum was carefully separated and placed into clean, tightly fitting plastic tubes before refrigerating at - 20°C until analysis. The animals were housed in private rooms, monitored, and independently evaluated by veterinary supervision in the facility. This study was completed following the Ain Shams University ethical research guidelines with [RE (209) 23] code number in experimental.

Biochemical analysis of serum: Complete Blood Count (CBC) was estimated according to [19]. Malondialdehyde (MDA), reduced glutathione (GSH), total antioxidant capacity (TAC), interleukin-6(IL-6), tumor necrosis factor-alpha (TNF-α), total cholesterol, triglycerides, HDL-C, and LDL-C were determined according to the methods described by [19,20, 21,22, 23,24], respectively.

Histopathological Examination: stomach tissue samples were taken from different rats in each group immediately after being sacrificed. The tissues were washed with the standard saline solution to remove blood, submerged in 10% neutral formalin as fixative, and sent to the Faculty of Veterinary Medicine for histopathological examination, according to [25].

Statistical Analysis: the data was statistically evaluated using automated SPSS software (SAS Institute, Cary, NC). The effects of various treatments were examined using a one-way ANOVA (Analysis of

variance) test with Duncan's multiple range test and p significance between different groups [26].

Results

Table 1 showed a significant decrease in the control (+ve) group compared to the control (-ve) group, and there was a non-significant change between other groups and the control negative group in body weight gain, feed intake, and feed efficiency ratio. The best result was noticed in the Curcumin oil group, which was closest to the control (-ve) group.

Table (1): Effect of using Curcumin, Thyme, and Chamomile oils on Body weight gain, food intake, and feed efficiency in ulcerated rats.

Groups / Parameters	Body weight gain	Feed intake FI (g)	Feed efficiency ratio %
Control (-ve)	19.50 ± 2.16^a	20.1 ± 3.16^a	0.040 ± 0.00^a
Control (+ve)	11.00 ± 1.25^c	15.2 ± 1.16^c	0.026 ± 0.00^c
Curcumin oil group	18.83 ± 3.30^a	19.8 ± 2.71^a	0.037 ± 0.00^a
Thyme oil group	16.68 ± 2.77^{ab}	17.4 ± 2.65^{ab}	0.032 ± 0.00^{ab}
Chamomile oil group	16.67 ± 2.31^{ab}	17.2 ± 2.36^{ab}	0.030 ± 0.00^{ab}

All data are expressed as the mean ± SD. Values in each column with different letters are significantly different ($p<0.05$).

Table 2 illustrated results for reduced glutathione (GSH); there was a significant decrease in the control (+ve) group compared to the control (-ve) group, while there was a significant increase in groups that had Curcumin oil, Thyme oil, and Chamomile oil compared to the control (+ve) group in (GSH). Along the same line, there was a significant increase in the control (+ve) group compared to the control (-ve) group in malondialdehyde (MDA) due to the induction with gastric ulcer. However, there was a non-significant change between both groups that had Curcumin, Thyme oil, and Chamomile oil, respectively, in (MDA) compared to the control (-ve) group in (MDA).

Furthermore, a notable significant rise in the (IL6) levels was observed in the control (+ve) group as compared to the control (-ve) group. There was a non-significant change between both groups that had Curcumin oil and Thyme oil in interleukin 6. However, there is a significant decline in the group that had Chamomile oil compared to the control (+ve) group in (IL6). In the same line, there was a significant increase in the control positive group (+ve) compared to the control negative group in tumor necrosis factor (TNF-α). The best result was noticed in Chamomile oil group compared to the control (-ve) group of (TNF-α) followed by Curcumin and Thyme oil groups. There was a significant decrease in the control (+ve) group compared to the control (-

ve) group in total antioxidant capacity (TAC). However, there was a non-significant change between all treated groups compared to the control negative group in (TAC).

Table (2): Reduced Glutathione (GSH), Malondialdehyde (MDA), Interleukin 6 (IL6), Tumor Necrosis Factor Alpha (TNF-α), and Total Antioxidant Capacity (TAC) results in various groups.

Groups / Parameters	GSH pg/ml	MDA ng/ml	IL6 pg/ml	TNF-α pg/ml	TAC U/ml
Control (-ve)	179.11 ± 6.39^a	21.9 ± 2.9^b	83.85 ± 2.4^b	37.61 ± 0.77^c	116.13 ± 9.08^a
Control (+ve)	53.40 ± 2.05^c	56.5 ± 1.44^a	139.7 ± 8.85^a	160.70 ± 6.42^a	48.61 ± 1.21^c
Curcumin oil group	162.0 ± 6.70^{ab}	24.4 ± 2.22^b	82.1 ± 3.64^b	46.60 ± 2.24^b	99.34 ± 3.86^a
Thyme oil group	156.0 ± 8.55^b	27.9 ± 2.38^b	90.95 ± 3.73^b	47.80 ± 2.28^b	95.60 ± 3.42^{ab}
Chamomile oil group	159.28 ± 7.05^b	18.05 ± 1.34^{bc}	69.35 ± 2.4^c	37.48 ± 1.40^c	111.2 ± 6.24^a

All data are expressed as the mean ± SD. Values in each column with different letters are significantly different ($p<0.05$).

Table 3 demonstrated results for Cholesterol (CHO), High-Density Lipoprotein Cholesterol (HDL-C), Low-Density Lipoprotein Cholesterol (LDL-C), and Triglycerides (TG), where there was a significant increase of the control (+ve) group in (CHO), (LDL-C), and (TG), compared to control (-ve) group. Also, there was a significant decline in (HDL-C) of the control (+ve) group compared to the control (-ve) group. There was a non-significant difference between all treated groups compared to the control (-ve) group.

Table (3): The effect of using Curcumin, Thyme, and chamomile oils on serum lipid parameters in indomethacin-induced gastric ulcer rats in various groups.

Groups / Parameters	Cholesterol mg/dl	HDL/ C mg/dl	LDL/ C Mg/dl	Triglycerides mg/dl
Control (-ve)	50.50 ± 0.76^b	40.0 ± 2.22^a	21.53 ± 1.29^{bc}	49.43 ± 3.12^{bc}
Control (+ve)	105.0 ± 1.53^a	24.5 ± 0.33^b	67.0 ± 1.74^a	116.5 ± 1.42^a
Curcumin oil group	55.37 ± 2.08^b	38.45 ± 2.96^a	24.50 ± 2.01^b	56.43 ± 3.28^b
Thyme oil group	53.93 ± 4.30^b	36.53 ± 2.68^a	26.13 ± 2.50^b	56.88 ± 2.81^b
Chamomile oil group	51.0 ± 0.44^b	37.83 ± 1.46^a	26.50 ± 0.54^b	51.50 ± 2.54^b

All data are expressed as the mean ± SD. Values in each column with different letters are significantly different ($p<0.05$).

Table 4 showed the results for hemoglobin (Hb), red blood cells (RBCs), and hematocrit (HCT), where there was a non-significant difference between groups that had Curcumin oil, Thyme oil, and Chamomile oil compared to the control (-ve) group.

Table (4): Hemoglobin (Hb), red blood cells (RBCs), and hematocrit (HCT) results in indomethacin-induced gastric ulcer rats in various groups.

Groups / Parameters	Hemoglobin g/dl	RBCs Millions/cm	HCT %
Control (-ve)	14.54 ± 1.13^a	7.49 ± 0.59^a	37.86 ± 2.92^a
Control (+ve)	13.05 ± 0.62^a	6.99 ± 0.37^a	34.08 ± 1.54^a
Curcumin oil group	13.88 ± 0.43^a	7.64 ± 0.41^a	38.10 ± 1.77^a
Thyme oil group	14.10 ± 0.32^a	7.17 ± 0.18^a	35.76 ± 0.84^a
Chamomile oil group	12.93 ± 0.18^a	7.08 ± 0.12^a	33.73 ± 0.57^a

All data are expressed as the mean ± SD. Values in each column with different letters are significantly different (p<0.05).

Table 5 showed that the results for mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), platelet count, and white cell count, where there was a non-significant difference between groups that had Curcumin oil, Thyme oil, and Chamomile oil compared to control negative group. But also, there was a significant decrease of the control (+ve) group compared to the control (-ve) group in platelet count and white cell count.

Table (5): The effect of using Curcumin, Thyme, and chamomile oils on mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), platelet count, and white cell count in indomethacin-induced gastric ulcer rats in-various groups.

Groups / Parameters	MCV FI	MCH Pg	Platelet count Thousands/cm	White cell count Thousands/cm
Control (-ve)	50.68 ± 0.33^a	19.42 ± 0.20^a	789.25 ± 22.93^a	21.66 ± 2.93^a
Control (+ve)	49.13 ± 0.82^a	18.73 ± 0.20^a	490.00 ± 47.52^c	13.08 ± 0.94^c
Curcumin oil group	50.35 ± 1.12^a	18.45 ± 0.63^a	752.67 ± 22.60^a	17.55 ± 0.80^{ab}
Thyme oil group	50.26 ± 1.77^a	18.98 ± 0.30^a	694.00 ± 24.32^{ab}	20.58 ± 2.72^a
Chamomile oil group	47.45 ± 0.01^a	18.73 ± 0.28^a	648.67 ± 27.72^{ab}	22.70 ± 2.53^a

All data are expressed as the mean ± SD. Values in each column with different letters are significantly different (p<0.05).

Table 6 showed that neutrophils, lymphocytes, monocytes, eosinophils, and basophils had non-significant differences between groups that had turmeric oil, thyme oil, and Chamomile oil compared to the control negative group. But also, there was a significant decrease between the control positive group and the control negative group in neutrophils.

Table (6): neutrophils, lymphocytes, monocytes, eosinophils, and basophils of indomethacin-induced gastric ulcer rats in various groups.

Groups / Parameters	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %
Control (-ve)	13.10 ± 1.34^a	71.30 ± 2.23^a	13.70 ± 1.03^{ab}	2.78 ± 0.05^a	0.2 ± 0.00^a
Control (+ve)	7.00 ± 0.74^c	75.08 ± 1.48^a	15.20 ± 1.15^a	2.78 ± 0.03^a	0.2 ± 0.00^a
Curcumin oil group	9.14 ± 1.48^{ab}	70.30 ± 4.43^a	13.43 ± 1.25^{ab}	2.80 ± 0.00^a	0.18 ± 0.01^a
Thyme oil group	11.18 ± 3.26^a	73.44 ± 4.74^a	12.06 ± 1.88^{ab}	2.79 ± 0.05^a	0.2 ± 0.00^a
Chamomile oil group	14.80 ± 1.83^a	71.53 ± 3.30^a	12.30 ± 0.17^{ab}	2.80 ± 0.00^a	0.2 ± 0.00^a

All data are expressed as the mean ± SD. Values in each column with different letters are significantly different (p<0.05).
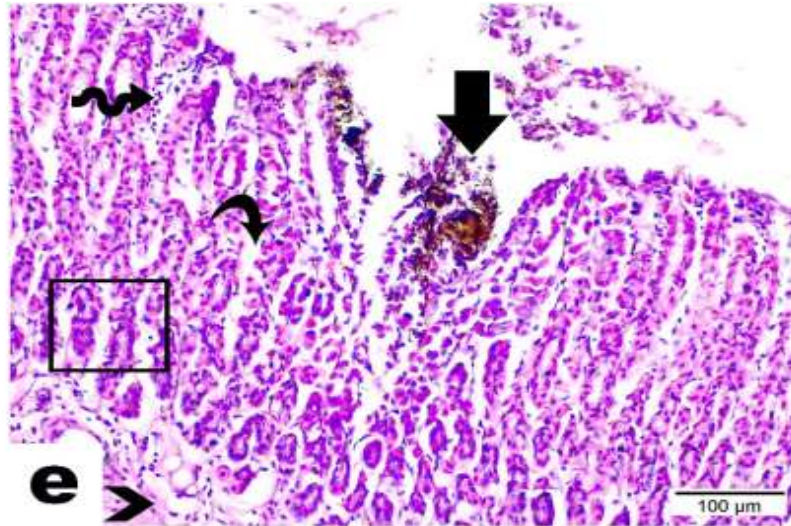
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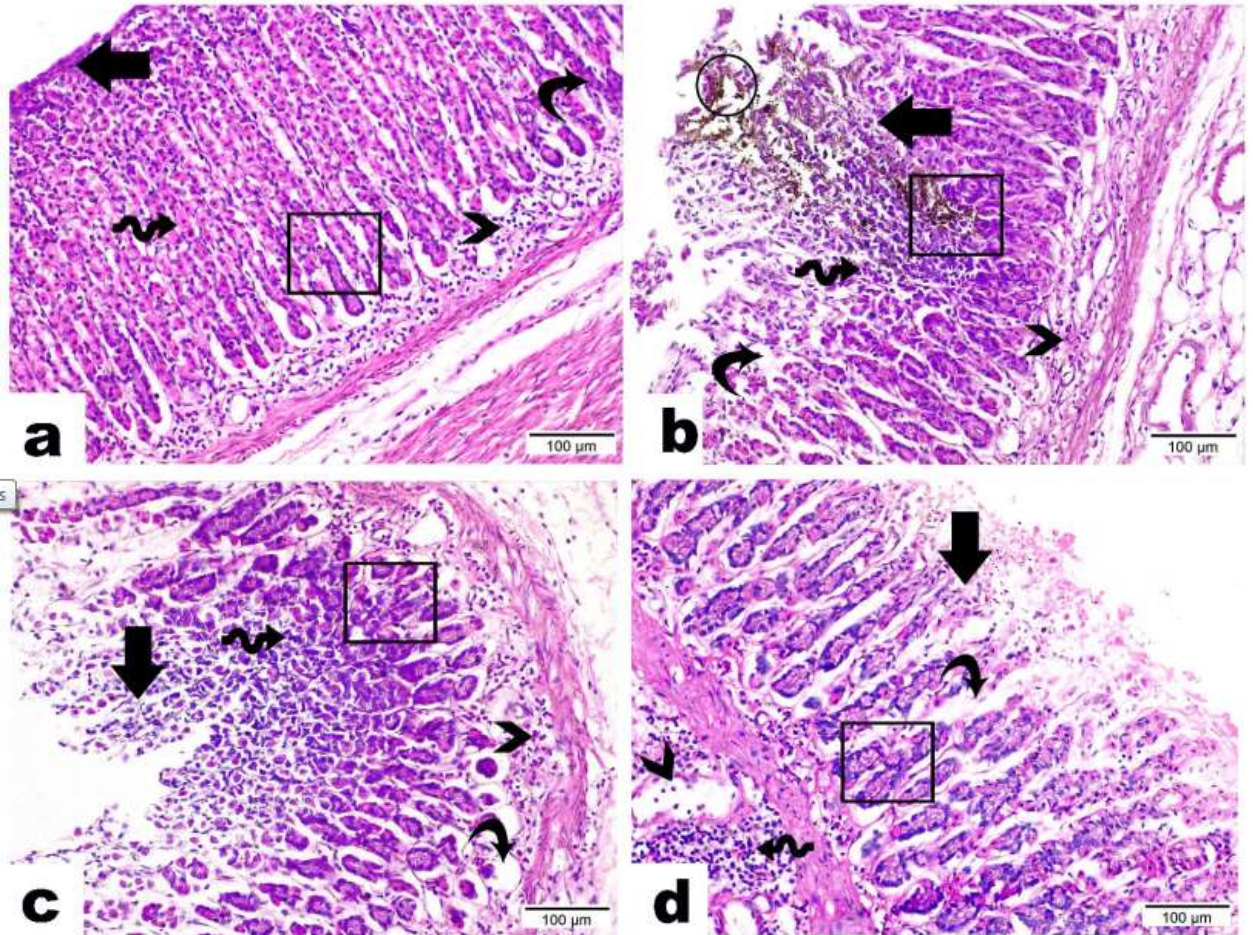
Figure Legend No. (1): Photomicrographs represented the histopathological alterations in stomach tissue sections between studied groups (Hematoxylin & Eosin Stain, Magnification Power= x200 & Scale Bar= 100μm)

(a) Stomach Section from Control Negative Group signifying the standard histological architecture of fundic region that assembled in intact lining epithelium (arrow), regular glandular structure (rectangle) with standard acidophilic parietal cell, (wave arrow) and basophilic chief cells (curvy arrow). Moreover, the usual presentation of lamina propria (arrowhead) was noticed.

(b) Stomach Section from Control Positive Group highlighting severe degenerative changes (arrow) evidenced as ulcerated epithelium with necrotic debris and hemosiderin pigment clumps (circle), loss of gland organization (rectangle), high aggregation of inflammatory cells along epithelium (wave arrow) as well as lamina propria (arrowhead), and interstitial edema (curvy arrows).

(c) Stomach Section from Curcuma Oil Protective Group revealing ulcerated epithelium with loss of normal structure (arrow). Some fundic glands appeared regularly (rectangle), and others had edema and apoptotic lining cells (curvy arrow). Aggregation of inflammatory cells along epithelium (wave arrow) and lamina propria (arrowhead) was also observed.

(d) Stomach Section from Thymus Oil Treated Group disclosing less degenerated epithelium (arrow), intact fundic gland organization (rectangle) with moderate interstitial edema in between (curvy arrow), and massive accumulation of inflammatory cells (wave arrow) along with dilated blood capillaries (arrowhead) in the submucosal layer.

(e) Stomach Section from Chamomile Oil Treated Group demonstrating limited area with ulcerated epithelium and necrotic debris

(arrow), intact fundic gland organization (rectangle) with minimal interstitial edema (curvy arrow) and few inflammatory cells aggregation in between glands (wave arrow) as well as along lamina propria (arrowhead).

Discussion

4.1. Body weight gain, food intake, and feed efficiency ratio

Weight is considered the primary indication for intestinal inflammation and medicine prevention and treatment of inflammatory lesions in animal modeling [27]. Indomethacin (INDO) is a non-steroidal medication; it has been previously claimed to possess a multitude of pharmacological actions., such as anti-inflammatory activity. Also, both rats and humans have a variety of gastrointestinal side effects. [28]. [29] proved a non-significant change in body weight gain and food intake after injection with indomethacin. Inversely, [30] illustrated that the indomethacin-treated rats stopped growth on the second day of drug inductions, the same result in our study, due to the effect of this drug on appetite and weight.

4.2. Reduced glutathione (GSH), malondialdehyde(MDA), interleukin 6 (IL6), tumor necrosis factor-alpha (TNF-α), and total antioxidant (TAC)

In gastric juice, most non-steroidal anti-inflammatory drug NSAIDs are weakly acidic, non-ionized, and lipophilic, which may elicit cytotoxic effects, resulting in cell death and compromising the integrity of the epithelial cell layer [31]. Cyclooxygenase (COX) serves as a crucial enzyme that regulates the rate of synthesis for eicosanoids. The two isoforms, namely COX-1 and COX-2, perform essential roles as enzymes in the metabolic pathway of arachidonic acid to the intermediate prostaglandins. [32]. COX-1 was found in almost all tissues and had a consistent appearance. It was primarily in charge of producing Prostaglandins (PGs), which help maintain stomach safety and enhance repairing ulcers. COX-1 has the potential to decrease the production of prostaglandin (PG) synthesis in the stomach mucosa and induce a deterioration in the defensive mechanism of the gut mucosa, which leads to the development of gastric mucosal erosion, ulcers, and several other forms of damage. [33].

According to [34], there was a significant increase of malodialdehyde (MDA) and a decline in the content of antioxidants because of side effects of using indomethacin; that was in agreement with our study. In the same line, [35] stated that (MDA) concentration increased in the indomethacin ulcerated group. Reduced glutathione (GSH) is an essential enzyme that scavenges superoxide anion radicals

and protects cells from oxidative damage [36]. Similarly, [37] reported that INDO raises interleukin (IL6) and tumor necrosis factor enormously.

On the other hand, [38] revealed that there was a notable reduction in interleukin 6 (IL6) and tumor necrosis factor-alpha (TNF-α) after treatment with chamomile oil due to its anti-inflammatory, antioxidative, and sedative effects of Chamomile and its major components (apigenin, azulene, and bisabolol) [13]. According to [39], NSAID-induced generates oxygen free radicals and pro-inflammatory factors, such as tumor necrosis factor-alpha (TNF-α). Also, [40] demonstrated that the mechanism occurred because of gastrointestinal damage caused by NSAIDs that influence (PG) inhibition and lead to gastric ulcer. Also, [41] reported that INDO negatively affected total antioxidant capacity compared to the control (-ve) group due to its mechanism stated above.

4.3. Cholesterol (CHO), High-density lipoprotein cholesterol (HDL-C), Low-density lipoprotein cholesterol (LDL-C), and Triglycerides (TG)

Indomethacin (INDO) is widely used in the management of inflammatory conditions, including rheumatoid arthritis and osteoarthritis.; however, there is evidence indicating a correlation between the consumption of this substance and the occurrence of gastrointestinal adverse reactions in both rats and human beings. [28]. In agreement with [41], there was a significant decrease in (CHO), (LDL-C), and (TG). On the other hand, there was a significant increase in (HDL-C) due to the effects of INDO on total lipids, as [41] illustrated this point. In agreement with this finding, [42] reported that the use of Thyme oil exhibits a notable reduction in Cholesterol and Triglyceride levels in quails due to its medicinal attributes and characterized in detail anti-inflammatory mechanisms [43].

Similarly, [44] mentioned that Thyme oil deliberates the activity of the cholesterol-synthesizing enzyme Hydroxymethylglutaryl Coenzyme A reductase and thereby leads to a decline in (CHO). In the same line, [45] Thyme oil elevates the concentration of (HDL-C), in agreement with [46], who reported the vital effect of Thyme oil on reducing (LDL-C) and (TG) that leads to an increase of (HDL-C) and protects the body from any inflammatory. The same result [47] proved that Curcumin oil due to its contents of a group of essential oils, which mainly consists of more than 250 diverse terpenoids identified from *Curcuma* species [48]. Also, Orellana-Paucar, [49] mentioned that the main constituents include Curcumin, curcuminoids, aromatic–turmerone, α-turmerone, β-turmerone, α-atlantone, arcurcumene, γ-curcumene, curlone, p-cymene, bisabolanes, guaianes, germacranes, caranes, elemanes, spironolactones, selinanes, santalanes, and caryophyllanes. As the same line, [50] stated

that Curcumin oil had a variety of medicinal properties, including anti-inflammatory properties.

4.4. Influence of natural oils on Complete Blood Count (CBC)

[51] demonstrated that there was a significant decrease in hematological parameters Red blood cells (RBCs), Hematocrit (HCT), Mean corpuscular Volume (MCV), mean corpuscular hemoglobin (MCH), platelet count and white cell count due to indomethacin side effects. Indomethacin is considered a main factor for the occurrence of gastric ulcer after prolonged use of it. On the other hand, [52] demonstrated that the antioxidant activity of Chamomile oil participated in overcoming gastric ulcer and moderated the complete blood count levels. Similarly, [50] stated that Curcumin oil is recognized to have numerous medicinal properties, including anti-inflammatory and anti-ulcer properties.

4.5. Histopathological alterations in stomach tissue

The non-steroidal anti-inflammatory drug cause ulcer model was considered one of the most common gastric ulcer models [53]. Moreover, indomethacin is frequently used in the management of inflammatory conditions, including rheumatoid arthritis and osteoarthritis. However, research has demonstrated that both rats and humans may experience gastrointestinal side effects as a result of its administration. [28]. In the same line, [54] mentioned that indomethacin affected stomach tissue where severe erosion, ulceration in the mucosa, and severe necrosis and hemorrhage occurred. In agreement with our study, indomethacin affected stomach tissue and caused gastric ulcer.

Conclusion

Natural oils with high antioxidant content, such as turmeric oil, thyme oil, and chamomile oil, could protect the stomach mucosa against indomethacin-induced harm. Its gastro-protective effects could be attributed to its ability to reduce the severity of aggressive factor-induced gastric mucosal damage and improve the morphological composition of stomach mucosa cells, as well as its boosting of antioxidant parameters, suppression of an excessive inflammatory response, and suppression of the lipid peroxidation marker risk. Natural oils may improve prostaglandin synthesis by increasing COX-1 and COX-2 expression in stomach tissues in rats.

This study indicated that natural oils had a favorable effect on indomethacin-induced stomach ulcers and confirmed a superior gastro-protective effect at a dose of 1ml/kg/ body weight, giving a significant perspective for the use of turmeric oil, thyme oil, and chamomile oil in the treatment of stomach ulcers caused by non-steroidal anti-inflammatory drugs (NSAIDs). More research is needed to study the

potential protective impact of natural oils on ulcerative lesions in the lower digestive tract and discover the best supplemental dose of natural oils in humans and their therapeutic uses.

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