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A physiological Study to the Effect of Astaxanthin in Female Albino Rats Induced with Gastric Ulcer by Aspirin

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Abstract

Background: Blood cells and their mediators in addition to antioxidants enzymes have essential role in physiology of gastric ulcer. Present study aimed to evaluate role of malondialdehyde (MDA), superoxide dismutase (SOD), prostaglandin E2 (PGE2) and fibroblast growth factor (FGF2) in addition to blood cells in aspirin induced gastric ulcer. **Method:** Gastric ulcer was induced in all experimental groups of females albino rats except the negative control group by dosing all groups with aspirin at a concentration of (100 mg/kg). Animals with gastric ulcer divided to groups and each group dosed by one of the astaxanthin (50 mg/k), omeprazole (20mg/ml) and mix of astaxanthin (50 mg/k)/ omeprazole (20mg/ml) and astaxanthin (75 mg/k)/ omeprazole (20mg/ml) for 21 day. Serological test preformed by ELISA assay for determine serum level of MDA, SOD, PGE2 and FGF2. Complete blood count were examined using the device (XP300 - Sysmex Analyzer Blood Auto). **Results:** The results of the current study showed a significant decrease ($P<0.05$) in RBC, WBC, MDA, SOD, PGE2 and FGF2 in the positive control group (T1) compared to the negative control group C in the first and second weeks of treatment. Astaxanthin have significant role in regulation of studied physiological markers that increased in gastric ulcer especially in second week of treatment therefore we need more studies about role of astaxanthin in healing of gastric ulcer.

Keywords: Astaxanthin, Gastric ulcer, Blood cells, MDA, SOD, PGE2, FGF2

Introduction

Gastric ulcers are bruises in the mucosa of the stomach lining, which ordinarily causes extreme stomach torment. The normal variables incorporate improper utilization of ibuprofen, a nonsteroidal calming drug (NSAID) [1], and Helicobacter pylori contamination [2]. Moreover, gastric ulcers are brought about by cigarette smoking, unnecessary drinking, or even pressure from day to day existence [3]. Lately, gastric ulcer has become one of the most widely recognized ongoing illnesses of the upper gastrointestinal parcel overall [4].

The primary medicines for gastric ulcers incorporate receptor blockers, anti-infection agents, and proton-siphon inhibitors (PPIs) [2]. Drugs, like omeprazole, pantoprazole, and lansoprazole, are ridiculously used to treat gastric ulcers by

expanding the gastric pH, subsequently permitting the mucosa to recuperate [5]. Notwithstanding, broad treatment with anti-microbials and long haul utilization of PPIs lead to an expansion in disappointment rates because of antimicrobial opposition and expected unfavorable impacts, including debilitated assimilation of supplements, intestinal contaminations, dementia, and different sicknesses [6,7]. In this manner, there is a dire requirement for the advancement of elective restorative specialists with few unfavorable aftereffects for treating gastric ulcers. In this review, we endeavor to decide job of Astaxanthin as remedial specialists all through assessment consequences for a few physiological markers present in instances of gastric ulcer .

Responsive oxygen species (ROS) are profoundly receptive particles that are delivered by the incomplete decrease of oxygen [8]. Cells endogenously produce ROS as side-effects of typical cell action, for example, mitochondrial oxidative digestion, xenobiotics digestion, and bacterial contamination [9]. Under physiological circumstances, ROS fixations are firmly controlled to gastric ulcer. At ordinary intracellular focuses, ROS goes about as a redox flagging courier, expected for various essential cell capabilities including cell separation, expansion, development, and apoptosis [10]. Cells are equipped with antioxidative enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX), as well as non-enzymatic anti-oxidants such as vitamin C and E, and polyphenols [11]. When Turf catalyzes the transformation of superoxide anion extremist to hydrogen peroxide, car or GPX further lessens hydrogen peroxide to water. In the event that these guard components are upset, it causes a lopsidedness between ROS creation and expulsion, which brings about oxidative pressure [12]. Elevated degrees of oxidative pressure can cause the obliteration of cell layers, lipid oxidation, and DNA harm in stomach tissues [10].

Reactive oxygen species (ROS) are highly reactive molecules that are produced by the partial reduction of oxygen [8]. Cells endogenously produce ROS as byproducts of normal cellular activity such as mitochondrial oxidative metabolism, xenobiotics metabolism, and bacterial infection [9]. Under physiological conditions, ROS concentrations are tightly regulated to gastric ulcer. At normal intracellular concentrations, ROS acts as a redox signaling messenger, required for a number of pivotal cellular functions including cell differentiation, proliferation, growth, and apoptosis [10]. Cells are equipped with antioxidative enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX), as well as non-enzymatic anti-oxidants such as vitamin C and E, and polyphenols [11]. Once SOD catalyzes the conversion of superoxide anion radical to hydrogen peroxide, catalase or GPX further reduces hydrogen peroxide to water. If these defense mechanisms are disturbed, it causes an imbalance between ROS production and removal, which results in oxidative stress [12]. High levels of oxidative stress can cause the destruction of cellular membranes, lipid oxidation, and DNA damage in stomach tissues [10].

Astaxanthin is a fat-solvent xanthophyll carotenoid that is normally present in Green growth, yeast, salmon, shrimp, and krill [13]. Normal wellsprings of regular

astaxanthin incorporate the green growth Haematococcus pluvialis and the red yeast Phaffia rhodozyma [14]. In the GI, astaxanthin has been accounted for to apply defensive impacts by diminishing bacterial burden, adjusting safe reaction, and repressing disease cell multiplication [15-17]. These advantageous impacts of astaxanthin are for the most part because of its powerful enemy of oxidant and mitigating movement, which is much more noteworthy than similar exercises in different carotenoids, for example, lutein and zeaxanthin [18]. Taking into account . Thus, astaxanthin as a potential nutraceutical in GI illnesses, the momentum paper expects to feature late advances in astaxanthin research with an emphasis on its enemy of oxidant and calming impacts against ulcers all through assessment its consequences for blood cells, MDA, SOD, PGE2 and FGF2.

Material and Methods

Preparation of laboratory animals

This study was conducted in the animal house affiliated with the Department of Life Sciences at the College of Education / University of Al-Qadisiyah for the period from 9/1/2024 to 3/2024, and 63 female rats were used in this study, Albino rats, whose weights ranged between (180-250 g), and they were obtained from Babylon Governorate / Saddat Al-Hindiyah, where the animals were placed in plastic cages covered with tight, meshed metal covers, and the cages were furnished with clean wood shavings, and the cages were taken care of and cleaned two to three times a week and sterilized, as they were taken care of under laboratory conditions of good lighting about 11 hours of light and 13 hours of darkness and good ventilation and suitable temperatures between 22-25m, and were left for two weeks for the purpose of adaptation. As for feeding the animals, they were given water and manufactured fodder during the experiment period.

Aspirin solution preparation

Aspirin powder was prepared from a stockpile of it to obtain the required dose of 100 mg/kg body weight by dissolving (1 g of aspirin powder in) 100 ml of 1% carboxymethyl cellulose, then giving 1 ml per 100 g/animal weight [19].

Omeprazole solution preparation

Omeprazole was used as a treatment for aspirin-induced ulcers in female white rats, where the required dose (20 mg/kg) was prepared with 2.0 g of omeprazole in 100 ml of distilled water to become its concentration 2 mg/ml and was given 1 ml per 100 g/animal weight [20].

Astaxanthin solution preparation

The two doses (50) and (75) mg/kg of body weight of astaxanthin powder were used, which were obtained from the manufacturer (Tic.San.Sis Akvaryum Kimya) after dissolving the full daily dose of astaxanthin in distilled water, then Each animal was given a daily dose of 1 ml orally using a doser specifically designed for this purpose [21].

Experimental design

A. **The first main experiment:** Gastric ulcer was induced in (65) female white rats by treating them with aspirin at a dose of (100 mg/kg) 7 consecutive days after starving the animals for 14 hours before giving aspirin. Its occurrence in the rat groups was confirmed by measuring the pH value and comparing it with the control group.
B. **The second main experiment:** It involved divided white rats females into seven groups each group included 10 animals as in following groups:
    1. The first group (C): It is considered the negative control group and is given distilled water and standard feed only throughout the experiment period of 21 days.
    2. The second group (T1): It is considered the positive control group in which gastric ulcers were induced by aspirin without treatment for 21 day.
    3. The third group (T2): It included group of animals with gastric ulcers and it is treated with the drug omeprazole at a concentration of 20 mg/kg for 2 weeks after gastric ulcer induction (period of experiment 21 day).
    4. The fourth group (T3): It included a group of animals with gastric ulcer and treated with astaxanthin compound at a concentration of 50 mg/k for 2 weeks after gastric ulcer induction (period of experiment 21 day).
    5. The fifth group (T4): It included group of animals with gastric ulcer and treated with astaxanthin compound at a concentration of 75 mg/kg for 2 weeks after gastric ulcer induction (period of experiment 21 day).
    6. The sixth group (T5): It included group of animals with gastric ulcer and treated with both omeprazole at a concentration of 20 mg/kg and astaxanthin compound at a concentration of 50 mg/kg simultaneously for 2 weeks after gastric ulcer induction (period of experiment 21 day).
    7. The seventh group (T6): It included group of animals with gastric ulcer and treated with both omeprazole at a concentration of 20 mg/kg and astaxanthin at a concentration of 75 mg/kg simultaneously for 2 weeks after gastric ulcer induction (period of experiment 21 day).

Animal sacrifice and sample collection

After the experiment was completed, the animals were sacrificed by anesthetizing them with chloroform and blood samples were drawn directly from the heart using a 5 ml medical syringe. Then 2 ml were taken and placed in tubes containing an anticoagulant (EDTA) for the purpose of studying blood parameters. The remaining part was placed in tubes (tube Gel) not containing an anticoagulant in order to obtain a sufficient amount of serum after placing them in a centrifuge (3000 rpm) for 15 minutes. Then the serum was drawn using a micro pipette and placed in special Bendorf tubes and stored at -20°C for the purpose of measuring physiological parameters..

Hematologic parameters measurement

Blood parameters included calculating the total number of red blood cells and white blood cells and measuring the percentage of hemoglobin and the packed cell

volume. All of these parameters were examined using the device (XP300 – Sysmex Analyzer Blood Auto) by placing a sample of the drawn blood in the device, then all the results for the above parameters were recorded directly from the device.

Physiological parameters measurement

The studied physiological parameters (MDA, SOD, PGE2 and FGF2) were evaluated using ELISA assay of serum samples and the test was performed according to the manufacturer's protocol (BTLAB/ CHINA).

Statistical analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences, version 22, with Excel 2010, and a probability of less than 0.05 was considered statistically significant.

Results

The results of the current study showed a significant decrease ($P<0.05$) in the number of red blood cells (RBC) in the positive control group (T1) compared to the negative control group C in the first and second weeks of treatment. The results of the statistical analysis showed a significant decrease ($P<0.05$) in group T2 compared to group C and T1 in the first week, while the treatment results for groups T3 and T4 recorded a significant decrease ($P<0.05$) compared to group C in the first week and no significant differences ($P>0.05$) between the two groups compared to the positive control group (T1), while groups T5 and T6 recorded a significant increase ($P<0.05$) in the number of red blood cells compared to group T1 and at the same time showed a significant decrease ($P>0.05$) in the level of red blood cell count compared to group C in the first week of treatment, while the second treatment group recorded a significant decrease ($P>0.05$) compared to the other treatment groups.

In the second week of treatment, group T2's results showed a significant increase ($P<0.05$) over group T1 and no significant differences ($P>0.05$) between the same group and group C. Groups T3 and T4 also showed a significant increase ($P<0.05$) over group T1 and no significant differences ($P>0.05$) between these groups and group C, while groups T5 and T6 showed a significant decrease ($P<0.05$) over group T1 and no significant differences ($P>0.05$) between these groups and group C. Additionally, it was observed that during the first and second weeks of therapy, there were no significant differences ($P>0.05$) between the treatment groups (T2, T3, T4, T5, and T6), as indicated in Table (1).

The statistical analysis revealed that in the first and second weeks of treatment, there was a significant increase ($P<0.05$) in the total number of WBCs in group T1 compared to group C. Meanwhile, in the first week of treatment, group T2 and group T3 recorded a significant decrease ($P<0.05$) in the total number of WBCs compared to group T1 and no significant differences ($P>0.05$) were observed compared to group C. Similarly, the results of groups T4, T5, and T6 showed a significant decrease ($P<0.05$)

in the total number of WBCs compared to group T1 and no significant differences (P>0.05) were observed in comparison to group C.

In the second week of treatment, the results of T2 and group T3 showed a significant decrease (P<0.05) compared to group T1 and group C. The results of group T4 and T5 also indicated a significant decrease in the total number of WBCs (P<0.05) compared to group T1, while the results of these groups showed a significant increase (P<0.05) compared to the group C. group T6 witnessed a significant decrease (P<0.05) compared to T1 with no significant differences (P>0.05) between it and group C. The groups T3 and T6 showed a significant decrease (P<0.05) in WBCs compared to other groups.

Table (1): Effect of astaxanthin and omeprazole on some blood parameters (WBCs, RBCs) of animals with gastric ulcer

Treatment groups	RBC(Cell/ml x 10^6 Mean ± standard deviation		WBCs (Cell x10^3/ml) Mean ± standard deviation	
	First week	Second week	First week	Second week
C	**7.53±0.109Aa**	**7.62±0.12Aa**	**6.01±0.84Ba**	**6.61±0.65BCa**
T1	**6.25±0.07Ba**	**6.20±0.09Ba**	**8.47±0.74Aa**	**8.41±1.11Aba**
T2	**6.84±1.12Aba**	**7.72±0.07Aa**	**6.00±1.93Bb**	**7.29±0.62ABa**
T3	**6.87±0.11Aba**	**7.77±0.15Aa**	**4.64±0.72Ba**	**5.27±1.13Ca**
T4	**6.78±0.07Aba**	**7.36±0.38Aa**	**6.65±0.30Aba**	**7.19±1.13ABCb**
T5	**6.65±0.03Aba**	**7.52±0.04Aa**	**6.93±1.58Aba**	**7.63±0.44ABb**
T6	**6.69±0.21Aba**	**7.78±0.18Aa**	**6.80±0.33Aba**	**6.46±0.95BCb**
LSD	**0.984**		**2.12**	

***Capital letters indicate vertical statistical reading; small letters indicate horizontal statistical reading; different letters between any two groups indicate significant differences (P<0.05)**

The first week's serological results for MDA I showed that group T1's MDA level was significantly higher (P<0.05) than group C's. With the exception of group T5, which demonstrated a significant decrease (P<0.05) in the MDA level compared to group T1 with no significant differences (P>0.05) between it and group C, groups T2, T3, T4, and T6 recorded a decrease in the MDA level that did not reach the level of significance (P<0.05) compared to group T1 and a significant increase (P<0.05) compared to group C. Table (2) shows that T5 recorded the lowest value compared to the other treatment groups. The MDA level in group T1 was significantly higher (P<0.05) than in group C during the second week, while groups T2 and T6 had significantly lower (P<0.05) MDA levels than in group T1, with no significant changes (P>0.05) from group C. Groups T3, T4, and T5 had the lowest MDA level values when

compared to group T1, and their results were significantly lower (P<0.05) than those of group C.

The ELISA test results for SOD in the first week showed that group T1 had a significant decrease (P<0.05) in comparison to group C, while groups T2 and T3 had a increase in the level of this enzyme that did not reach the level of significance (P<0.05) in comparison to group T1 and a significant increase (P<0.05) in comparison to group C. However, the results of groups T3 and T4 showed a increase in comparison to group T1 that did not reach the level of significance (P<0.05), while the same group showed a significant decrease (P<0.05) in comparison to group C. In the first week of treatment, group T4 had the lowest value when compared to the other treatment groups, while group T5 and T6 recorded a significant increase (P>0.05) compared to T1 and a significant increase (P<0.05) compared to group C. At the same time, group T4 did not exhibit any significant differences (P>0.05) from group C.

The results of the statistical analysis in the second week of treatment showed a significant decrease (P<0.05) in the level of SOD in the T1 group compared to the C group and the other treatments except for the T2 group, which showed no significant differences (P>0.05) between it and the T1 group, while the T3 group recorded a significant increase (P<0.05) in the SOD level compared to the T1 group and the C group. While the results of the T4 group indicated a increase of the level of significance (P<0.05) in the level of SOD compared to the T1 group, while its increase remained significant (P<0.05) compared to the C group in the second week of treatment, while the T5 and T6 groups showed a significant increase (P<0.05) in the level of SOD compared to the T1 group and no significant differences (P>0.05) with the C group, while the T2 and T6 groups recorded the lowest value compared to the rest of the other treatments in the second week of treatment, as shown in Table (2).

Table (2): Effect of astaxanthin and omeprazole on some stress parameters (MDA, SOD) of animals with gastric ulce

Treatment groups	MDA (Nmol/L) Mean ± standard deviation		SOD (U/ml) Mean ± standard deviation	
	First week	Second week	First week	Second week
C	**2.62±0.54Ba**	**3.83±0.36Ba**	**6.50±0.49Ba**	**5.81±0.72Ba**
T1	**4.14±0.77Aa**	**5.15±0.22Aa**	**5.24±0.23Ba**	**5.18±0.18Ba**
T2	**3.80±0.40Aba**	**3.49±0.41BCDa**	**5.62±0.35Ba**	**6.81±0.36Aba**
T3	**3.41±0.17Aba**	**2.93±0.51BCDa**	**8.25±0.27Aa**	**6.59±0.48ABb**
T4	**3.21±0.27Aba**	**2.61±0.11CDa**	**7.15±0.55Aba**	**5.54±0.44Ba**
T5	**2.93±0.39Ba**	**2.37±0.33Da**	**6.96±1.79Aba**	**6.69±0.11Aba**
T6	**3.50±0.55Aba**	**3.69±0.19BCa**	**6.39±0.53Ba**	**6.91±0.15Aba**

LSD	**1.17**	**1.73**

***Capital letters indicate vertical statistical reading; small letters indicate horizontal statistical reading; different letters between any two groups indicate significant differences (P<0.05)**

The results of the ELISA analysis of PGE2 concentration in first and second weeks showed a significant decrease ($P<0.05$) in the level of PGE2 for group T2 compared to group C, while the results of group T2 recorded a significant increase ($P<0.05$) in the level of PGE2 compared to group T1 while the same group recorded no significant differences ($P>0.05$) compared to group C in the first week of treatment. Groups T3 and T6 witnessed a significant increase ($P<0.05$) compared to group T1 and no significant differences compared to group C.

The results of group T4 showed a significant increase ($P<0.05$) in the level of PGE2 compared to T2 ($P<0.05$), while the level of PGE2 was significantly high ($P<0.05$) compared to the negative control group C, and the T5 group showed the lowest significant value ($P<0.05$) in the level of PGE2 compared with control groups T1 and C in the first week of treatment, and at the same time recorded the lowest significant value compared with the other treatment groups in the first week of treatment as shown in Table (3). In the second week of treatment, The results of the statistical analysis also showed a significant decrease ($P<0.05$) in the level of PGE2 for group T2 compared to the negative control group (C) while the results of group (T3) and (T6) recorded a significant increase ($P<0.05$) in the level of PGE2 compared to the group (T1), with no significant differences ($P>0.05$) between the two groups and the group (C) in the second week of treatment while both the group (T4) and (T5) showed an increase that did not reach the level of significance ($P<0.05$) in the level of PGE2 compared to group (T1) and a significant decrease ($P<0.05$) compared to group (C) in the second week of treatment, at the same time, groups T4 and T5 recorded the lowest significant value compared with other treatment groups in the second week of treatment.

The statistical analysis revealed that the positive control group (T1) had a significantly higher level of FGF2 ($P<0.05$) than group C in the first and second weeks of treatment, while groups T2 and T5 had a significantly lower level of FGF2 ($P<0.05$) than groups T1 and C in the first week of treatment, and groups T3, T4, and T6 had a significantly lower level of FGF2 ($P<0.05$) than group T1. Groups T2 and T5 displayed the lowest significant value ($P<0.05$) in comparison to the other treatment groups in the first week of treatment, as indicated in Table (3). At the same time, the level of PGE2 among the three groups approached its level in group C, so we did not observe significant differences ($P>0.05$) in the first week of treatment.

The second treatment group T2 recorded a significant decrease ($P<0.05$) In the level of FGF2 compared with group T1, and at the same time, no significant differences were observed ($P>0.05$) compared with group C in the second week of treatment. The results of group T3 demonstrated a significant decrease ($P<0.05$) in the level of FGF2 compared with the T1 group, at the same time, the same group showed a significant increase ($P<0.05$) in the level of FGF2 compared with group C in the second week of treatment. Groups T4, T5 and T6 witnessed a significant decrease ($P<0.05$) in the level of FGF2 compared with group T2 whereas the same two groups showed a significant increase ($P<0.05$) in the level of FGF2 compared with the group C in the second week of treatment, while the results of group T2 reported the lowest significant value

(P<0.05) compared with the other treatment groups in the second week. as seen in Table (3).

Table (3): Effect of astaxanthin and omeprazole on PGE2 and FGF2 of animals with gastric ulcer.

Treatment groups	PGE2 (ng/ml) Mean ± standard deviation		FGF2 (ng/ml) Mean ± standard deviation	
	First week	Second week	First week	Second week
C	7.48±0.43Aa	5.81±0.24Ba	436.78±46.7Ca	539.24±63.5Ba
T1	4.52±1.12Ba	4.01±0.81CDa	715.79±19.87Ab	947.73±58.6Aa
T2	7.34±0.68Aa	5.79±0.29Ba	458.22±18.77Ca	528.15±18.5Bb
T3	8.27±0.24Aa	5.22±0.36BCb	577.47±68.66Ba	440.02±48.4Bb
T4	4.87±0.95Bb	8.47±0.35Aa	484.33±38.97BCa	456.34±34.7Ba
T5	4.79±0.62Ba	3.26±0.35Da	487.15±86BCa	582.50±24.1Bb
T6	7.28±0.39Aa	5.06±0.44BCb	488.57±47.02CBa	489.51±64.7Ba
LSD	1.61		104.6	

***Capital letters indicate vertical statistical reading; small letters indicate horizontal statistical reading; different letters between any two groups indicate significant differences (P<0.05)**

Discussion

The results of our study showed the ability of astaxanthin to restore the number of white and red blood cells to their normal level in animals with aspirin induced gastric ulcers. We also found a successful effect when using astaxanthin and omeprazole together in healing the ulcer through the effect of these compounds on regulating concentrations of MDA, SOD, PGE2 and FGF2 in the serum of experimental animals that had gastric ulcers induced using Aspirin. NSAIDs are commonly used analgesic agents due to their anti-inflammatory and painrelieving properties. They can induce some side effects such as ulcerative lesions in the GI tract [22,23]. In addition to being employed as a stimulant to study gastric antral ulcer models with erosions and petechial hemorrhage in the stomach mucosa, aspirin is frequently prescribed for patients with stroke or thrombosis [24]. Inflammation and regular physiological processes are both significantly mediated by prostaglandins. Aspirin and other NSAIDs block the enzyme that uses a two-step cyclo-oxygenation and peroxidation process to convert arachidonate to prostaglandin H2, which in turn inhibits the formation of prostaglandin E2 (PGE2) [25]. By controlling the number of blood cells and reversing the decreased activities of MDA, SOD, PGE2, and FGF2, as well as raising the lipid peroxide level to that of untreated normal rats, astaxanthin treatment demonstrated protective effects against aspirin-induced gastric ulcers in aspirin-treated rats [22–25]. According to Cao *et al*. (2014), supplementing with 10 mg of astaxanthin/kg of diet alleviates the negative effects of aflatoxin-B1 (AFB1) on hematological and serum parameters, as well as liver pathological changes in broilers [26]. Previous research has demonstrated that astaxanthin has anti-ulcer activity through its anti-oxidant and anti-

inflammatory effects. For antioxidant activity, astaxanthin increases the activity of antioxidant enzymes like glutathione peroxidase, superoxide dismutase, and catalase [27]. These enzymes lower the levels of reactive oxygen species, which raise the levels of lipid peroxides and 8-hydroxy-20-deoxyguanosin. ROS activate nuclear factor-κB (NF-κB) to induce the expression of inflammatory cytokines, such as interleukin (IL)-8, which causes dysregulated acid secretion, mucosal damage, and the recruitment of white blood cells in gastric mucosal tissues [27]. Astaxanthin prevents mucosal injury and these ROS-mediated changes. Furthermore, astaxanthin stimulates the production of SOD2, MDA, and catalase, which lowers ROS in gastric epithelial cells, via activating the peroxisome proliferator-activated receptor-γ (PPAR-γ) [28]. By changing the pro-inflammatory T helper type 1 (Th1) response in immune cells to an anti-inflammatory Th2 response, astaxanthin has antimicrobial action. It increases the subset of T and B cells and promotes mitogen-induced lymphoproliferation. As a result, astaxanthin inhibits the development of stomach ulcers [28].

According to Handa *et al.*, indomethacin, a non-corticosteroid medication, is also commonly utilized because of its anti-inflammatory, anti-pyretic, and analgesic properties [29]. However, it can have certain negative consequences, like erosions in the stomach mucosa and ulcerative sores. Astaxanthin (25 mg/kg BW; three days) enhanced the activities of SOD, CAT, and GPX, which offer protections against oxidative damage in the gastric mucosa, in rats with indomethacin-induced gastric mucosal injury. The study's findings indicate that astaxanthin avoided the gastric hemorrhagic lesions caused by indomethacin and eliminated the lipid peroxides and free radicals that were produced by the drug [29, 30].

Notably, the overall WBC count tends to rise during ulceration, which is consistent with earlier research on stomach ulcers [31]. Similar to this, Kondo *et al*., found that after gastric ulcers, particularly those caused by *H. pylori* infection, were successfully treated, the overall numbers of leucocytes, neutrophils, monocytes, and red blood cells in peripheral blood decreased [32]. Karttunen *et al.*, found that during gastric ulcer, the number of lymphocytes and basophils increased along with the WBC count, which may indicate the degree of inflammation of the gastric mucosa [33].

Conclusion

According to available data, astaxanthin's anti-inflammatory and antioxidant properties seem to promote healing and slow the development of stomach ulcers. Astaxanthin is an antioxidant that lowers oxidative stress, boosts NO bioavailability and antioxidant enzyme activity, and preserves the blood cells' rheological characteristics. Astaxanthin's advantageous safety profile and these characteristics make it a viable choice for the prevention and/or adjuvant therapy of stomach disorders.

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