Protective and Therapeutic Potential of a Novel Phytobiological Formulation of Nutrients in the Treatment of Indomethacin-Induced Gastric Ulcer

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Alamri *et al.*: Therapeutic Potential of Phytobiological Formulation in the Treatment of Indomethacin-Induced Gastric Ulcer

Gastric ulcers have been considered as a major problem worldwide. This study investigated the protective synergistic effect of a novel nutrient formulation for the protection and treatment of indomethacin-induced gastric ulcer in rat model. 24, 8 w old male rats with a body weight between 220 and 240 g, were divided into four groups and used for this study. Group 1 consists of healthy controls and group 2 consists of ulcerative animals, group 3 consists of ulcerative+phytobiological formulation treatment (80 mg/kg) and group 4 consists of omeprazole (40 mg/kg). Pre-treatment with 80 mg/kg of phytobiological formulation improved the activities of the measured antioxidant enzymes, decreased lipid peroxidation and inflammation, as evidenced by improved surface and glandular epithelium (white arrows) of phytobiological treated group stained with hematoxylin and eosin and tumor necrosis factor alpha immuno-expression when compared with the ulcer group. In conclusion, the mechanism by which this phytobiological formulation prevents indomethacin-induced gastric ulcer may be mediated *via* improving the homeostasis of enzymatic (superoxide dismutase) and nonenzymatic (glutathione) antioxidants, inhibiting (malondialdehyde) and decreasing the formation of inflammatory cytokines (tumor necrosis factor alpha, C-reactive protein content and interleukin-10). Consequently, this phytobiological formulation may be a beneficial nutrient formulation therapy for patients diagnosed with gastric ulceration.

Key words: Curcumin, resveratrol, green tea, quercetin, cruciferex, indomethacin, gastric ulcer

Gastric ulcers have been considered as a major problem worldwide. Around 70 % of the population in various developing countries, depend on conventional therapy for the treatment of ulcer conditions[1]. However, recent reports on the use of these conventional treatments have been increasingly associated with unpleasant side effects and in some instances, ineffective. Studies have shown that men are usually more at risk of developing ulcers than women with an incidence rate of around 10 % worldwide[2]. The occurrence of different types of ulcers are age dependent with duodenal ulcers occurring in men ranging in ages from 30-55 y, while gastric ulcers are more common in men ranging from 50-70 y in age[3]. Prolonged usage of drugs including aspirin and other anti-inflammatory drugs which are non-steroidal (Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)) may cause ulcers and other gastric lesions[2]. Those drugs inhibit the Cyclooxygenase (COX) enzyme which reduces the synthesis of cytoprotective endogenous prostaglandins thus rendering the mucosa susceptible to various dangerous products

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consequently resulting in the impairment of the host immune defense and repair mechanisms[3]. Among the prominent histopathological features associated with gastric ulceration, massive necrosis, gastritis, micro-erosion and hemorrhage are more common[4].

In developing countries, herbalists and traditional healers have been reported to use phytogenic candidates for gastric ulcers treatment. Also, the application of assorted phytobiological therapies have proven to yield improved outcomes with less side effects and lower drug resistance[5]. Consequently, in recent years several anti-ulcer research studies have been centered on the development of novel phytobiological formulations to serve as substitutes for conventional chemotherapeutic agents. Although several herbal and synthetic antioxidants have been investigated for this purpose there is a paucity of information on a definite combination formulation that can be supplemented to effectively prevent against gastric ulcers.

Curcumin ($C_{21}H_{20}O_6$) is a phenolic compound with Hydroxyl (OH) and Methyl (CH_2) groups in beta (β)-diketone moiety which are likely responsible for its antioxidant potency[6,7]. Aside being effective against many inflammatory diseases including gastric ulcers and with negligible side effects, curcumin is a very affordable and commonly found in many fruits and vegetables. In *in vivo* experimental studies curcumin was shown to enhance the efficacy of drugs used and reduced the side effects associated with the treatment[8]. It exerted its efficacy by restoring the function of the antioxidative enzymes[8,9].

Similarly, resveratrol a polyphenolic compound common in berries, grapes and peanuts has been reported to possess both anti-inflammatory properties and antioxidant potential to scavenge free radicals[10,11]. Resveratrol showed efficacy in the treatment and protection against ethanol mediated gastric ulcers in rats and this potential was attributed to its ability to inhibit neutrophil infiltration and other biological markers that are involved with inflammation[12].

Equally, green tea (*Camellia sinensis*) has high amounts of catechins which are flavonoids such as epigallocatechin gallate and epicatechins. Green tea is a scavenger of free radical and restores the oxidative system and protects it from damage due to its antioxidant properties[13]. Green tea extracts caused a modulation in the equilibrium of the oxidant/antioxidant levels and resulted in treatment of gastric ulcers[14].

Besides, quercetin is a common flavonoid antioxidant, anti-inflammatory agent that is synthesized by many plants like tea, onions and apples[15-18]. Quercetin is effective against *Helicobacter pylori*-induced ulcers[19] and demonstrated effectiveness and protection against gastric ulcers attributable to its antioxidant potential[20].

Also, certain nutrients have been associated with anti-ulcer effects. For instance, deficiency of water-soluble vitamins was associated with peptic ulcers. Protective effects against peptic and gastric ulcer were demonstrated by vitamins: vitamin B_6, vitamin C and E. Consequently, this study, evaluated the protective and therapeutic potential of a novel nutrient formulation composed of an assortment of vitamins, minerals, nutrients and antioxidants against indomethacin-induced gastric ulcer in rat model.

MATERIALS AND METHODS

Experimental design:

Animals: Male rats who were 8 w old with a body weight ranging from 220 to 240 g, served as subjects in this study. They were housed at 24° and 5 % relative humidity and offered a standard laboratory diet and *ad libitum* tap water for 1 w. Four groups (6 rats /group) of rats were used and each set was replicated three times. Group 1: Healthy controls; group 2: Ulcerative animals; group 3: Ulcerative+phytobiological formulation treatment (80 mg/kg) and group 4: Omeprazole (40 mg/kg). 36 h before commencing the experiment, all animals were deprived from food to ensure an empty stomach but had free access to water. During the study period the rats were housed individually in metabolic cages with elevated floors and wire mesh to minimize coprophagy. Animal ethical approval was obtained with the ethical approval number: ACUC-21-08-32.

Induction of gastric ulcer using indomethacin:

Gastric ulcer was induced in the ulcerative group using single dose of indomethacin (30 mg/kg body weight) dissolved in 3 % Tween 80 which was administered *via* oral intubation. While the control group received the same dose of 3 % Tween 80 dissolved in distilled water. Rats were treated for 2 d after the ulcer was induced. Group 3 received treatment with phytobiological formulation (80 mg/kg) by gastric gavage once daily for 10 d. 1 d before the administration of the last dose of the

test formulation, animals were weighted and then sacrificed by cervical dislocation which was done under humane conditions. Afterwards, stomachs were extracted and evaluated for mucosal damage and they are rated as such: Petechiae (intense moderate and light with 3, 2 and 1 points, respectively), hyperemia (1 point), edema (1 point), ulcers (perforated and not perforated, 2 point/mm^2 and 1 points/mm^2, respectively), thickening of the ulcer (1 point/mm^2) and hemorrhagic lesion (3 points)[21].

Ulcer inhibition rate: Control (ulcer index)-Test (ulcer index)×100 %/Control (ulcer index).

Assessment of kidney and liver function:

Serum concentrations of C-Reactive Protein (CRP), uric acid creatinine, Alanine Transaminase (ALT) and Aspartate Transaminase (AST), Alkaline Phosphatase (ALP), urea and Interleukin-10 (IL-10) MBS763996 were determined using Enzyme-Linked Immunosorbent Assay (ELISA) kits of MyBioSource (USA) catalogue number MBS9719084, MBS9719085, MBS2903804, MBS2600001 and MBS1600166 respectively, according to the manufacturer's instructions.

Preparation of samples for antioxidant determination:

A stomach portion samples was mixed with 2 % Triton X-100 with 0.32 M sucrose solution and homogenized for the assessment of Superoxide Dismutase (SOD). In the case of Malondialdehyde (MDA), another stomach part was added and homogenized in 50 mM potassium phosphate at pH 7.5 and in the presence of 1 mM Etheylenediamine Tetraacetic Acid (EDTA) for assaying MDA and Glutathione (GSH). The obtained homogenates were subjected at a temperature of 4° twice to sonication at 30 s intervals. This was followed by centrifugating the resulting homogenates for 10 min at 1800 g[22,23].

Reduced GSH assessment: GSH was assayed as previously described by Almasaudi *et al.* and the activity was expressed in nmol/g tissue[4].

Assessment of lipid peroxide (MDA): Depending on the method of Uchiyama and Mihara the concentration of MDA was assessed. This was done using Biodiagnostic kits, Egypt and the concentration presented as nmol/g tissue[24].

SOD activity: The SOD activity was analyzed using the Biodiagnostic kits, Egypt and presented in U/g tissue[25].

Determination of IL-10, Tumor Necrosis Factor alpha (TNF-α) and Nuclear Factor kappa B (NF-κB):

ELISA kits (Assaypro, United States of America (USA); MBS2507393), (Novex, USA; MBS825017) and (MyBioSource; USA; MBS268833) were used to measure the concentrations of TNF-α, IL-10 and NF-κB in stomach homogenates respectively. While the levels of cytokines were computed using standard purified recombinant cytokines following manufacturer's guidelines.

Histological and histochemical studies:

The gastric tissues were fixed in 4 % paraformaldehyde solution. For general histology studies, 5 μm thick tissues were dissected and exposed to Hematoxylin and Eosin (H and E) stain[26]. Periodic Acid-Schiff (PAS) staining was used to evaluate the polysaccharide condensation[27] and viewed under a light microscope.

Immunohistochemical studies:

Immunohistochemical staining for detection of TNF-α was done. The primary monoclonal antibodies used were the mouse anti-TNF-α (Santa Cruz Biotechnology, Santa Cruz, California, USA) 1:300 with Phosphate Buffered Saline (PBS). The cellular site of the reaction was the cytoplasm which appeared brown in color[28]. The avidin-biotin peroxidase method was used in the immunohistochemical study, which was followed by adding the chromogen, Diaminobenzidine (DAB) (Dakopatts, Glostrup, Denmark), to the slides. The latter were then washed with distilled water and counterstained using hematoxylin. The specific primary antibody was substituted by PBS in the case of the negative control[29].

Statistical analysis:

At the end of the study, the obtained data were presented as mean±Standard Error of the Mean ($\bar{x}$±SEM) and Analysis of Variance (ANOVA) and Tukey's post-hoc test was used to evaluate the differences among the groups. GraphPad Prism was used to analyze the data and values of $p < 0.05$ were recorded as statistically significant.

RESULTS AND DISCUSSION

Effect of phytobiological formulation on percentage (%) Body Weight Gain (BWG) was shown in Table 1. The administration of phytobiological formulation (80 mg/kg) did not produce a significant change of

BWG (p=0.879) as compared to the rats in other groups.

Effect of phytobiological formulation in indomethacin-induced gastric ulcer on liver and kidney function tests was shown in Table 2. The gastric mucosal level of ALT and AST, ALP, urea, uric acid and creatinine were significantly elevated compared to the control group (p≤0.01, 0.001, 0.004, 0.019 and 0.007, respectively). Phytobiological formulation (80 mg/kg) administered for 14 d caused a significant decrease in gastric mucosal uric acid, ALT, AST, urea, ALP and creatinine content as compared to the ulcer control group (p=0.001, 0.003, 0.002, 0.014, 0.037 and 0.028, respectively). No statistically significant difference was detected between the group treated with phytobiological formulation and that treated with omeprazole.

Effects of phytobiological formulation on oxidative stress parameters in gastric mucosal was shown in fig. 1. Administration of indomethacin resulted a significant reduction in GSH activity (75.3 %) as compared to the control contents (p=0.001, fig. 1A. Conversely, a significant increase (4.8-fold) in the gastric mucosal lipid peroxidation (MDA concentration) in the treatment of rats with indomethacin was observed in comparison to the controls (p=0.001, fig. 1B). Ulcer-induced rats pretreated with phytobiological formulation (80 mg/kg) showed significant increase in gastric mucosal GSH contents (2.2-fold) (p=0.006, fig. 1). Conversely, pretreatment of ulcer-induced rats with phytobiological formulation (80 mg/kg) significantly decreased gastric mucosal MDA concentrations (60.6 %) as compared to indomethacin injected rats (p=0.002) (fig. 2A and fig. 2B). The difference between the group treated with phytobiological formulation and that treated with omeprazole was not statistically significant.

Table 3 shows that treatment of rats with indomethacin caused a significant decrease in activities of both gastric mucosal SOD (53.5 %) and Catalase (CAT, 50.3 %) as compared to the control rats (p=0.001 and 0.003). Pretreatment of indomethacin-injected rats with phytobiological formulation significantly increased gastric mucosal SOD (1.5-fold) (p=0.004) and CAT enzyme activity (1.6-fold) (p=0.002). The difference between the groups treated with phytobiological formulation and that treated with omeprazole was not statistically significant.

Effect of phytobiological formulation in indomethacin-induced gastric ulcer on gastric mucosa proinflammatory cytokines was shown in Table 4. Treatment of rats with indomethacin caused a significant increase in TNF-α and CRP levels (2.6 and 3.8-fold, respectively) (p=0.001, and 0.001, respectively) in comparison to the control. Pretreatment of indomethacin-injected rats with phytobiological formulation (80 mg/kg) caused a significant decrease in plasma TNF-α and CRP (32.6 % and 63.2 %) (p=0.006 and 0.002) as compared to the ulcer-induced rats. No significant difference was observed between the group treated with phytobiological formulation and that treated with omeprazole (Table 4).

Sections from rat stomach showing effect of phytobiological formulation (80 mg/kg) on gastric mucosa stained with H and E were shown in fig. 3A-fig. 3D. The IL-10 levels in the gastric mucosa was significantly decreased (62.7 %) in comparison to the control group (p=0.001). The treatment of rats with phytobiological formulation (80 mg/kg) significantly increased gastric mucosal IL-10 levels (2.7-fold) in comparison to the ulcer control (p=0.001) and there was normal intact epithelium (white arrows) in control group as shown in fig. 3A.

TABLE 1: EFFECT OF PHYTOBIOLOGICAL FORMULATION ON BWG

Treatment regimen	BWG	
	Mean	SEM
Control	12.39	0.89
Phytobiological formulation (80 mg/kg)	12.67	0.56
Ulcerative	11.7	0.7
Omeprazole (40 mg/kg)	12	0.62

Note: Data are expressed as mean±SEM (n=6 in each group) and analyzed by independent t-test

TABLE 2: EFFECT OF PHYTOBIOLOGICAL FORMULATION ON LIVER AND KIDNEY FUNCTION TEST PARAMETERS IN INDOMETHACIN-INDUCED GASTRIC ULCER

Treatment regimen	ALT (U\l)	AST (U\l)	ALP (IU/l)	Serum urea (mg/dl)	Uric acid (mg/dl)	Serum creatinine (mg/d)
Control	16.70±0.78	19.23±2.53	43.39±2.51	14.57±1.92	5.97±0.98	0.69±0.71
Ulcerative	74.97±6.50[a]	109.43±9.36[a]	138.38±11.9[a]	53.53±4.81[a]	9.08±0.95[a]	2.56±0.78[a]
Phytobiological formulation (80 mg/kg)	33.33±5.13[ab]	39.33±5.51[ab]	59.33±4.73[b]	20.13±1.53[b]	6.50±1.731[b]	1.09±0.32[b]
Omeprazole (40 mg/kg)	26.90±0.78[ab]	33.23±2.53[ab]	53.39±4.51[b]	18.57±1.92[b]	6.90±0.98[b]	0.99±0.71[b]
p value	<0.001	<0.001	<0.001	<0.001	0.022	0.007

Note: Data are expressed as mean±SEM (n=6 in each group) and analyzed by ANOVA followed by Tukey's test; [a]Significantly different from the value in the control group (p<0.05); [b]Significantly different from the value in the ulcerative group (p<0.05)
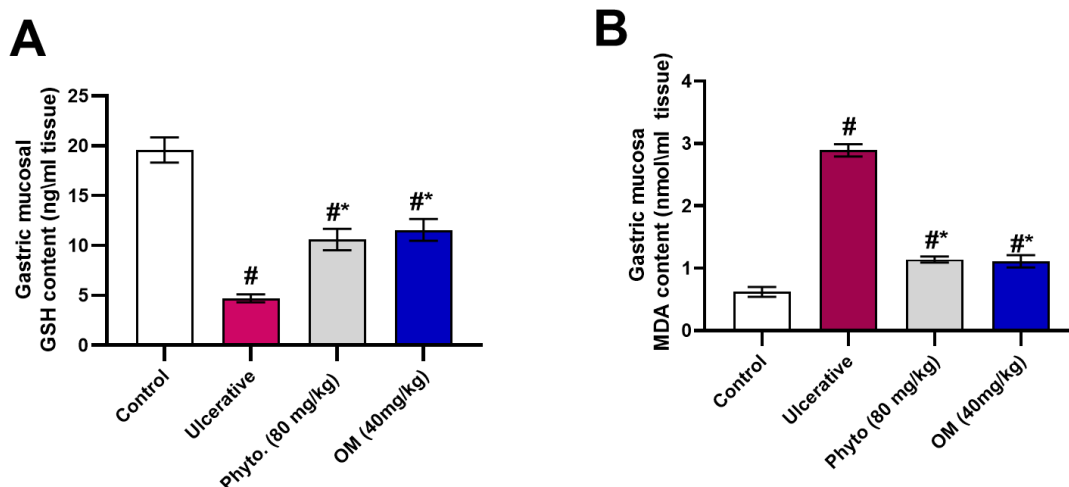

Fig. 1: Effect of phytobiological formulation (80 mg/kg) on gastric mucosa, (A) Reduced GSH content and (B) MDA concentration as compared to the ulcer and control groups
Note: Each value is represented as mean±SEM (n=6), Phyto: Phytobiological formulation group and OM: Omeprazole group, #Significant *vs.* control (p≤0.05) and *Significant *vs.* indomethacin-induced gastric ulcer (p≤0.05)
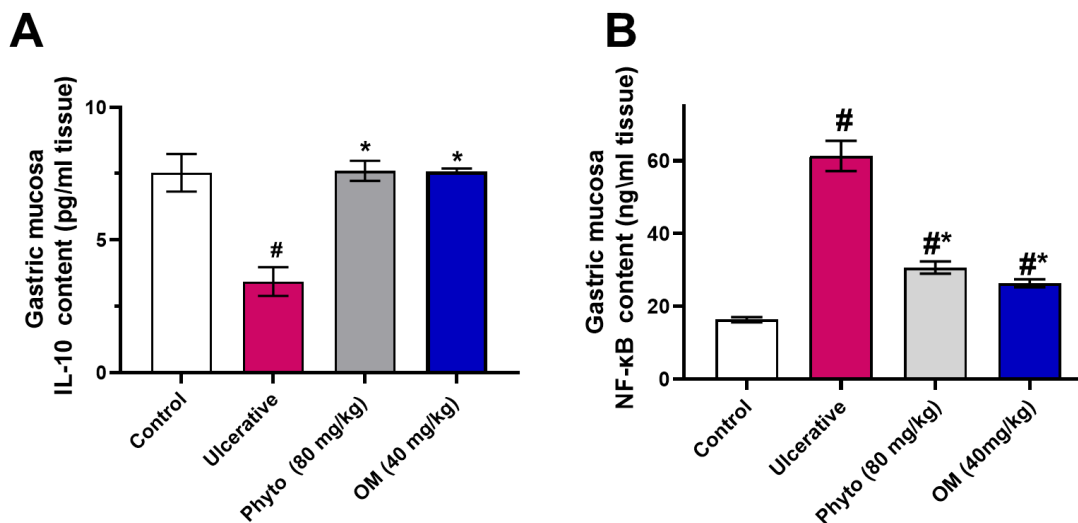

Fig. 2: Effect of phytobiological formulation (80 mg/kg) on gastric mucosa (A) IL-10 and (B) NF-κB levels, compared to the ulcer and control groups
Note: Each value is represented as mean±SEM (n=6), Phyto: Phytobiological formulation group and OM: Omeprazole group, #Significant *vs.* control (p≤0.05) and *Significant *vs.* indomethacin-induced gastric ulcer (p≤0.05)

TABLE 3: EFFECT OF PHYTOBIOLOGICAL FORMULATION ON SOD AND CAT ACTIVITIES MEASURED IN INDOMETHACIN-INDUCED GASTRIC ULCER IN RATS

Treatment regimen	SOD (U\ml tissue)	CAT (mU\l tissue)
Control	183.47±4.02	124.05±2.05
Ulcerative	85.17±13.54[a]	61.77±2.51[a]
Phytobiological formulation (80 mg/kg)	132.08±9.17[ab]	102.33±7.2[b]
Omeprazole (40 mg/kg)	143.47±2.02[ab]	104.05±2.05[b]
p value	<0.001	<0.001

Note: Data are expressed as mean±SEM (n=6 in each group) and analyzed by ANOVA followed by Tukey's test; [a]Significantly different from the value in the control group (p<0.05); [b]Significantly different from the value in the ulcerative group (p<0.05)

TABLE 4: EFFECT OF PHYTOBIOLOGICAL FORMULATION (143 mg/kg) ON GASTRIC MUCOSA TNF-α AND CRP LEVEL MEASURED IN INDOMETHACIN-INDUCED GASTRIC ULCER IN RATS

Treatment regimen	TNF-pg/ml tissue)	CRP (pg/ml tissue)
Control	16.40±0.96	6.57±1.56
Ulcerative	43.70±2.80[a]	23.33±5.03[a]
Phytobiological formulation (80 mg/kg)	29.30±5.54[ab]	8.67±1.53[b]
Omeprazole (40 mg/kg)	23.47±2.02[b]	104.05±2.05[b]
p value	<0.001	<0.001

Note: Data are expressed as mean±SEM (n=6 in each group) and analyzed by ANOVA followed by Tukey's test; [a]Significantly different from the value in the control group (p<0.05); [b]Significantly different from the value in the ulcerative group (p<0.05)
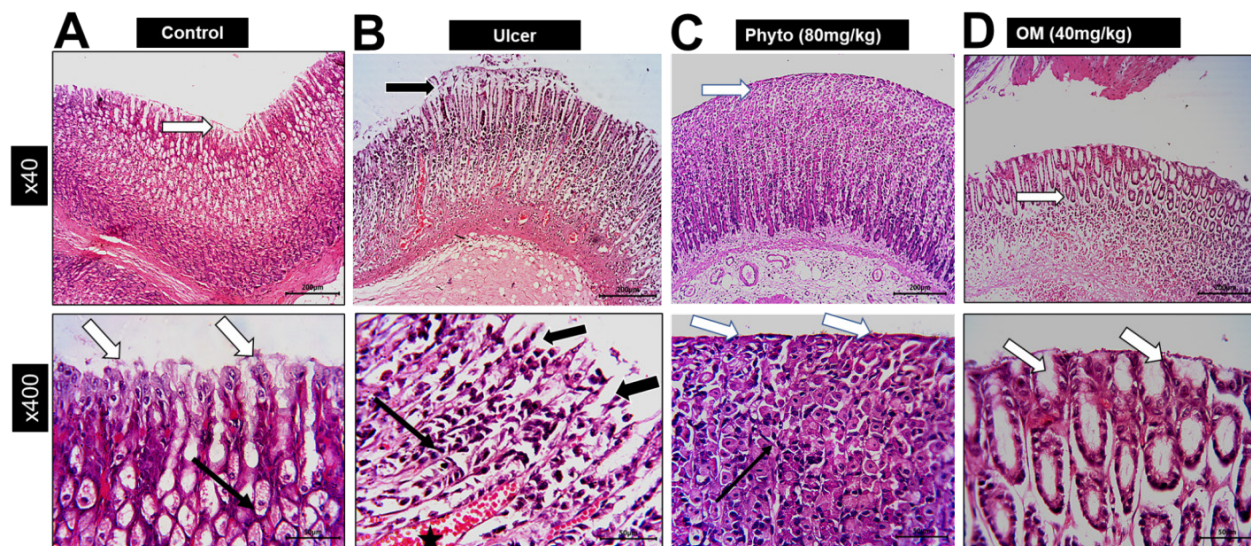

Fig. 3: Sections from rat stomach showing effect of phytobiological formulation (80 mg/kg) on gastric mucosa stained with H and E
Note: (A) Control group; (B) Ulcer group; (C) Phytobiological group (80 mg/kg) and (D) Omeprazole group (40 mg/kg)

A significant increase in the gastric mucosa NF-κB activity (2.6-fold) was observed in the ulcer control group in comparison to the control group (p=0.001). A significant reduction in the gastric mucosa NF-κB activity was detected in the phytobiological formulation (80 mg/kg) treated group (69.6 %) as compared to ulcer control group (p=0.004). No significant difference was observed between the group treated with phytobiological formulation and that treated with omeprazole.

There was marked surface epithelium loss (black arrows) and degeneration of glandular epithelium (distorted glandular cells with dark pyknotic nuclei) with vascular congestion (star) in ulcer group (fig. 3B). Preservation of surface epithelium and deep glandular epithelium also showed potential preserved structure in phytobiological group, similar to the control group (white arrows) was shown in fig. 3C and preservation of surface and deep glandular epithelial structures (white arrows) in omeprazole

group was shown in fig. 3D. Pre-administration of phytobiological formulation (80 mg/kg) provided good preservation of stomach mucosal structures against indomethacin-induced ulceration, both surface epithelium and glandular elements looked intact with less degenerative changes similar to the omeprazole group.

TNF-α immuno-stained sections from rat stomach showing effect of phytobiological formulation (80 mg/kg) on gastric mucosa was shown in fig. 4.

We found that marked decrease in TNF-α immuno-expression in the preserved surface and glandular epithelium (white arrows) in control group was shown in fig. 4A. Increase in TNF-α immuno-expression in degenerated glandular cells of ulcer model (black arrows) was found in fig. 4B. Decrease in TNF-α immuno-expression in the preserved surface and glandular epithelium (white arrows) in phytobiological group was found in fig. 4C and marked decrease in TNF-α immuno-expression in the preserved surface and glandular epithelium (white arrows) in the omeprazole group was compared to ulcer model as shown in fig. 4D. Pre-administration of phytobiological formulation (80 mg/kg) provided potential good preservation of stomach mucosal structures against indomethacin-induced ulceration, both surface epithelium and glandular elements looked intact with less degenerative changes similar to the omeprazole group.

In the recent years, phytobiological therapies have yielded promising results against gastric ulcer. Consequently, we thought it exciting to investigate the protective and therapeutic potential of administering a novel phytobiological formulation (consisting of curcumin, resveratrol, green tea extract, quercetin and cruciferex) in indomethacin-induced gastric ulcer. Data obtained from this study showed that the indomethacin administration results in severe gastric hemorrhagic erosions. Indomethacin has been reported to lead to mucosal injury by inducing gastric damage *via* inhibiting the release of protective factors like bicarbonate, Prostaglandin E2 (PGE2), COX-1 and mucus, increasing oxidant parameters while decreasing activities of antioxidant enzymes[30]. Pre-treatment with 80 mg/kg of phytobiological formulation improved the activities of the measured antioxidant enzymes, decreased lipid peroxidation and inflammation, as evidenced by improved surface and glandular epithelium. This is the first study to report improvement in gastric ulceration following administration of a novel phytobiological formulation (consisting of curcumin, resveratrol, green tea extract, quercetin and cruciferex) against indomethacin-induced gastric ulcer.
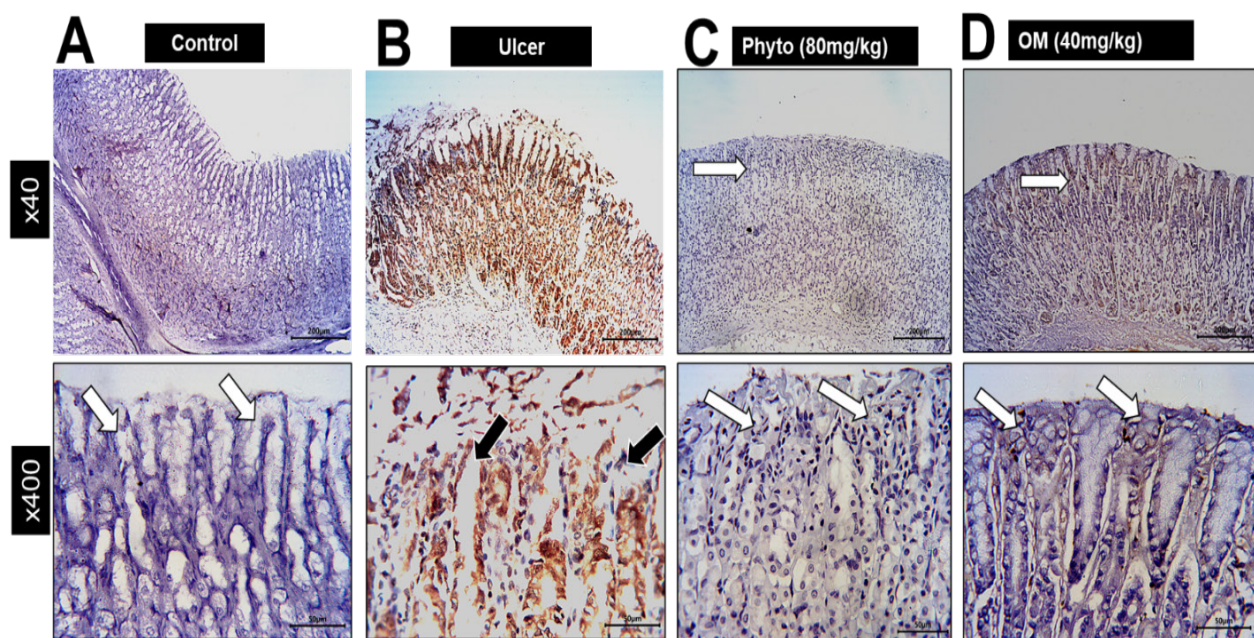

Fig. 4: TNF-α immuno-stained sections from rat stomach showing effect of phytobiological formulation (80 mg/kg) on gastric mucosa
Note: (A) Control group; (B) Ulcer group; (C) Phytobiological group (80 mg/kg) and (D) Omeprazole group (40 mg/kg)

In the observation, we found that administration of phytobiological formulation did not produce any significant decrease in BWG, which suggests that it is safe and non-toxic to the animals.

Antioxidants have been shown to prevent mucosal injury and gastric damage *via* scavenging intra and extracellular superoxide radicals and hydrogen peroxides thereby preventing damage to cell constituents or activation of microglia *via* acting as intracellular second messengers. Treatment with our novel phytobiological formulation considerably increased the activities of oxidative stress-related enzymes and stabilized the concentration of MDA, thus signifying its anti-peroxidative potential. The significant decrease in MDA observed in the group treated with phytobiological formulation, compared to the ulcer group indicates that this nutrient formulation yields an improved outcome in ameliorating the adverse effects of gastric ulcer, induced *via* increased lipid peroxidation[30-32]. The result of the present study also agrees with those of previous studies reporting that supplementation with individual formulations combined in our novel nutrient formulation is found to be effective in scavenging free radicals[1,5,7,10,15,17,18,20,33].

In the observation that pretreatment with phytobiological formulation yielded significant decrease in plasma TNF-α, CRP and gastric mucosa NF-κB activity, while gastric mucosal IL-10 levels were increased which suggests that this novel nutrient formulation potently stabilized the biochemical parameters in the ulcerated rats as no significant difference was observed between the group treated with phytobiological formulation and that treated with conventional therapy (omeprazole). The potential of this phytobiological formulation to alleviate the biochemical hallmarks of gastric ulcer can also be attributed to its synergistic antioxidant potential of the individual formulation comprised in this nutrient formulation. This corroborates previous reports suggesting that at physiologic doses exogenous antioxidants can re-establish or sustain the redox homeostasis, a vital factor responsible for maintaining the biochemical homeostasis in different systems[8,14,21,30]. Photomicrograph of gastric tissue section stained with H and E and TNF-α immuno-stained sections of rats with gastric ulcer pre-treated with phytobiological formulation showed little degenerative epithelial cells, decreased TNF-α immuno-expression and preserved surface and glandular epithelium like the omeprazole group. This phytobiological formulation resulted in the modulation of COX-pathway and mediated its efficacy by the upregulation of the levels of the mucosal growth factors and sustaining the balance between the anti and pro-inflammatory cytokines to enhance ulcer healing[10,15,20,30,31].

Overall, the result of the present study demonstrates that supplementation with this phytobiological formulation may possess beneficial antioxidant properties for populations susceptible to gastric ulcer.

In summary, the result from this study further highlights the potential anti-ulcer activity of a novel phytobiological formulation (consisting of curcumin, resveratrol, green tea extract, quercetin and cruciferex) in indomethacin-induced gastric ulcer in rat model. The mechanism by which this phytobiological formulation exerts its effect may be mediated *via* improving the homeostasis of enzymatic (SOD) and nonenzymatic (GSH) antioxidants, inhibiting MDA and decreasing the formation of inflammatory cytokines (TNF-α, CRP content and IL-10). Consequently, this phytobiological formulation may be a beneficial therapy for patients diagnosed with gastric ulceration.

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Conflict of interests:

The authors declared no conflict of interest.

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