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Poliansature Fosfotidilkolinin (PFK) Stres Ülser Gelişimini Engellemedeki Etkinlik Mekanizmaları

The Protective Effect Mechanisms of Polyenylphosphatidylcholine (PPC) Pretreatment Against Stress Induced Ulcer in Rats

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Özet

GİRİŞ ve AMAÇ: PPC ile prolifilaksinin, stres ülser gelişimini engellemede etkin olduğu daha önce yapılan deneysel bir çalışmada gösterilmiştir. Yine rat stres ülser modelinde gerçekleştirilen bu deneysel çalışmada, bu etkinliğin altında yatan mekanizmaların araştırılması amaçlanmıştır.

YÖNTEM ve GEREÇLER: Ratlar, Grup1 (n=10) kontrol, Grup2 (n=15) stres ülser ve Grup3 (n=15) PFK tedavisi + stres ülser olmak üzere üç gruba ayrıldı. Stres ülser modeli için Grup 2 ve grup 3 ratlar, 72 saatlik açlık periyodundan sonra, immobilize halde, +4 C?de, 4 saat soğuğa maruz bırakıldı. Grup 3 ratlara, PFK 100 mg/gün dozunda, oral yoldan, deney öncesi 10 gün süreyle verildi. Deney periyodu sonunda total çıkartılan ve büyük kurvatur boyunca açılan midelerde okülometrik yöntemle ülser indeksi (UI) hesaplandı Gastrik doku örneklerinde malondialdehit (MDA) ve superoksit dismutaz (SOD), glutatyon (GSH), ksantin oksidaz (XO), eritrositlerde katalaz (CAT), plazma örneklerinde ise total nitrit+nitrat, prostaglandin E2 (PGE2) ve lökotrien C4 (LTC4) düzeyleri ölçüldü. Histopatolojik incelemede gastrik mukozal hasar (H&E boyama) ve mast hücre degranülasyonu (dominici boyama) değerlendirildi.

BULGULAR: Ülser indeksi (UI)' nin PFK ile profilaksi grubunda, grup 2'den anlamlı düzeyde düşük olduğu görüldü (p<0,000). PPC verilen 3. grupta 2. gruba göre MDA, XO, total nitrit+nitrat ve LTC4 düşük (p< 0,000), SOD, GSH, CAT ve PGE2 anlamlı düzeyde yüksek (p<0,000) bulundu. Histopatolojik incelemede grup 3 ratlarda mast hücre degranülasyonu (özellkle mavi boyanan mukozal mast hücrelerinde), grup 2 ratlara göre anlamlı düzeyde düşüktü (p<0,000).

TARTIŞMA ve SONUÇ: Çalışmamızda, PFK' nin, rat stres ülser modelinde, antioksidan, mast hücre degranülasyonunu önleyici, LTC4 üretimini azaltıp PGE4 üretimini arttırıcı etkinliklere sahip olduğu, stres ülser gelişimini engellemesinde bu mekanizmaların rol oynadığı düşünülmüştür.

Anahtar Kelimeler: Stres ülser, Fosfotidilkolin, Prostaglandin E2, Lökotrien C4, Mast hücre degarnülasyonu

Abstract

INTRODUCTION: This study aims to investigate the mechanisms that are involved in protective actions exerted by pretreatment with polyenylphosphatidylcholine (PPC) against experimentally induced stress ulcer in rats.

METHODS: Forty Swiss albino rats were divided into three groups. Group 1 (n=10) was control, group 2 (n=15) was stress ulcer and group 3 (n=15) was PPC treated rats with stress ulcer. PPC treatment was started ten days before stress at a dose of 100 mg/day by oral route. Rats were terminated, stomachs were excised. Macroscopic ulcer index (UI), production of reactive oxygen species, lipid peroxidation, plasma PGE2 and LTC4 levels, fatty-acid compositions were studied. The specimens were examined histopathologically.

RESULTS: UI was significantly lower in the treatment group compared with non-treatment group. PGE2 decreased (p=0.00) during cold restraint stress. PPC pretreatment was observed to inhibit the decrease in PGE2 in the induced stress ulcer. In the PPC treatment group LTC4 levels were significantly lower than non-treatment group (p=0.00). Additionally, PPC pretreatment inhibited degranülation of the submucosal mast cells. The inhibitory effect of PPC was more potent on red- stained mast cells than on blue-stained cells.

DISCUSSION AND CONCLUSION: The present study shows that protective effects of PPC could be ascribed to inhibition of mast cell degranulation, a reduction in gastric oxidative injury, increase in biosynthesis of protective PGE2, and a decrease in biosynthesis of LTC4.

Keywords: Stress ulcer, Polyenylphosphatidylcholine, Prostaglandin E2, Leukotreine C4, Mast cell degranulation

INTRODUCTION

Stress ulcerations develop in patients with sepsis, major trauma and after major surgeries complicated with shock and sepsis (1). Stress ulcerations are multiple superficial injuries

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surrounded by little even no inflammatory reaction. These lesions are always found in the body of the stomach however they may spread distally to involve the antral mucosa. Althogh various hypotheses have been proposed, the precise biochemical changes during stress ulcer generation are not clear yet. Increased gastric motility, vagal over activity, mast cell degranulation, decreased gastric mucosal blood flow, and decreased prostaglandin levels during stress condition are thought to be involved in ulcer generation (2-3). Recently, attention has been focused on the role of reactive oxygen species (ROS) in the development of stress ulcers (4). Oxygen-derived free radicals have been shown in stress ulcers. It has been shown that stress-ınduced gastric lesions to be caused mainly by oxidative stress owing to ROS (5).

The polyenylphosphatidylcholine (PPC) study medication (Essentiale forte) contained a soybean lecithin extract which is termed "essential" phospholipids (EPL), consisting of 72%-%76 phosphatidyl-choline of which the two major species are dilinoleoylphosphatidyl-choline (32%-42%) and palmitoyl-linoleoyl-phosphatidylcholine (18%-19%). In our previous study, it was shown that PPC pretreatment has a protective effect on stress induced ulcer formation in rats (6). In the present study, we attempted to clarify whether PPC pretreatment is protective or not against cold-restraint stress (CRS) induced acute mucosal lesions in rats by examining the changes in the mast cell degranulation and heterogeneity in gastric tissue; and changes in the plasma prostaglandin E_2 and leukotreine C_4 levels during CRS.

MATERIAL AND METHODS

Experimental Design

The study was approved by the İnönü University Ethical Committee for Experimental Animal Research (2003\10).

Forty Swiss albino rats of either sex weighing 180 to 200 g were used in the experiment. The animals were left 7 days for acclimatization to animal room conditions and maintained on standart pellet diet and water ad libitum. The food was, however, withdrawn 72 h before the experiment, but the animal was allowed free access of water. The animals were divided into three groups. The first group was control group (n=10). In the second group (non-treatment, CRS), animals were induced stress ulcer and treated with saline (n=15). The third group (treatment, CRS+PPC) consisted of stress ulcer induced rats that were pretreated with PPC (n=15). PPC preparation, Essentiale® forte N (Aventis Pharma, Deutschland GmbH, Nattermannallee 1, 50829 Köln) was administered orally to the rats in the group 3 in a daily dose of 100 mg for ten days before experiment (7).

Animal Preparation

The rats were immobilized in the supine position in the light ether anesthesia by tying the fore and hind limbs to four pins of a wooden board.[7] After recovery from anesthesia, they were kept at 4°C for 4 hours. Control group was kept at room temperature for similar period of time. At the end of the 4 hoursof experimental period, blood samples were taken by intracardiac puncture under ether anesthesia and the animals were sacrificed.

Assessment of Gastric Mucosal Damage (Ulcer Index)

The stomach was opened along the greater curvature, washed with distile water, and pinned out flat in standard position for macroscopic examination and scoring of ulcer with the help dissecting microscope (X 10). Lesion size was determined by measuring each lesion along its greatest diameter; in the case of petechial lesions, five such lesions were considered the equivalent of a 1 mm ulcer. The sum of the total

severity scores in each group of rats divided by the number of animals was expressed as the mean ulcer index (UI). The inhibition percentage was calculated by the formula (7):

[(UInon-treated – UItreated)/ UInon-treated] x 100

Examination of mast cells in gastric wall

Gastric tissues were fixed 10 % formalin and embedded in paraffin. Serial sections (5 µm thick) from each block were cut 30 µm apart. Sections were stained with alcian blue-safranin to demonstrate the histochemical heterogeneity of mast cell and their degree of degranulation. Mast cell counts were expressed as the number of granulated metachromatically stained mast cell seen in 40 adjacent oil immersion fields (magnification 400x) in the following areas: 1) immediately below and parallel to the mucosal surface epithelium (mucosal count), 2) in the submucosa (submucosal count) and 3) in the muscle (muscularis propria count)(Olympus CH 30), X400) (8).

Determination oxidants (Xanthine oxidase (XO), total nitrite-nitrate), anti-oxidants (Superoxide dismutase (SOD), gluthatione (GSH), catalase (CAT)) and lipidperoxidation

For determination of lipid peroxidation in tested groups, tissue levels of malondialdehyde (MDA) were measured. Tissue MDA levels were determined by the method described Uchiyama et al.[10] Briefly, MDA was reacted with thiobarbituric acid by incubating for 1 hour at 95° to 100°C. After the reaction, spectrophotometric intensity was measured in the n-butanol phase by comparing with a standard solution 1.1.3.3. tetramethoxypropane. Results were expressed in terms of nanomole per gram wet tissue.

Tissue XO activities were measured by the method of Prajda and Weber (11), where the activity is measured by determination of uric acid from xanthine. Quantitation of nitrite and nitrate was based on the Griess reaction. Total nitrite (nitrite +nitrate) was measured by spectrophotometry at 540nm (12).

Catalase (EC 1.11.1.6) activity was determined according to Aebi's method (13). The principle of the method was based on determination of the rate constant *k* (s−1) of the H_2O_2 decomposition rate at 240 nm. Results were expressed as k per g tissue protein.

The rat gastric tissues (0.5 g) was homogenized in 3 mL of tricholoroacetic acid solution and centrifuged at 10,000×g for 5 min at 4°C. The obtained supernant fraction was analyzed for total GSH using the enzymatic method which was based on the use of Ellman's reagent (14). Results were expressed µmol/gwet tissue. Total (Cu–Zn and Mn) SOD (EC 1.15.1.1) activity was determined according to the method of Sun *et al* [15]. The principle of the method is based on the inhibition of NBT reduction by the xanthine–xanthine oxidase system as a superoxide generator. One unit of SOD was defined as the enzyme amount causing 50% inhibition in the NBT reduction rate. The SOD activity was also expressed as U g^{-1}protein.

Measurement of PGE_2 and LTC_4

After ethyl acetat extraction (20°C, 4-12 h), the samples were centrifuged (10,000 × *g* for 15 min), the supernatants were collected and the ethanol in the samples evaporated under a stream of N_2. The remaining solutions were acidified to pH 4 with HCl and the prostaglandins and leukotrienes extracted by three sequential treatments with 2 × (v:v) ethyl acetate. After evaporation to dryness, the residue was resuspended in ELISA buffer (Amersham) for enzyme-linked immunosorbent assay. Each condition was tested in triplicate. PGE_2 and LTC4 were determined using ELISA (for PGE_2 and LTC_4 levels RPN222 RPN224 cod number kits, respectively Amersham Bioscience UK), using ELISA according to the manufacturer'sprotocol (16).

Fatty acid analysis

Non-esterified plasma fatty acids were quantified by one-step rapid extractive methylation for gas chromatographic analysis as described previously (17-18). First, citrate plasma was spiked with heptadecanoic acid as internal standard. Next, free fatty acids were converted to methyl esters by mixing with ethereal diazomethane. Lastly, the ethereal layer was dried, redissolved in chloroform, and transferred to the gas chromatograph. An isolated control group consisting of 10 rats was created to show the effects of ten days PPC treatment (in a daily dose of 100 mg) on plasma fatty acid composition. The plasma fatty acid composition of this group at the end of ten days PPC administration was depicted in Table 3.

Histopathologic examination

For histological assessment, samples were obtained from the stomach, fixed in 10% formalin, embedded in paraffin. Sections from tissue blocks taken from ulcerated areas were stained with hematoxylin-eosin (H&E) for routine histologicexaminations (8-9).

Statistical analysis

All statistical analyses were carried out using SPSS statistical software (SPSS for windows; Chicago, IL, USA). Means and standart error mean(SEMs) were calculated for all data. Significant differences between means were evaluated by Kruskal-Wallis analysis and in the case of significance; Mann-Whitney U-test was also applied. P values less than 0.05 were considered to be significant.

RESULTS

Ulcer Index

Exposure of the rats to cold restraint stress at 4°C for four hours induce severe mucosal erosion and hemorrhagic ulcer in the glandular portion of the stomach all of the animals with group 2 (Figure 1A). These ulcers varied from pin-point erosions (petechia) to elongated bands ranging from 1 to 24 mm in length. PPC pretreatment for a ten days period before stress, significantly prevented from the formation of gastric mucosal lesions induced by CRS ($p<0.05$)(Figure 1B). Stomachs of eleven out of fifteen in the treated group were completely protected from any damage. PPC pretreatment inhibited the cold-restraint induced stress ulcerogenesis in 96.4 % (inhibition percentage) (Table 1). Kruskal-Wallis analysis of variance indicated the significant differences of incidence, number and length of petechia and erosions and UI between the treated and non-treated groups ($p<0$ .00) (Table 1).

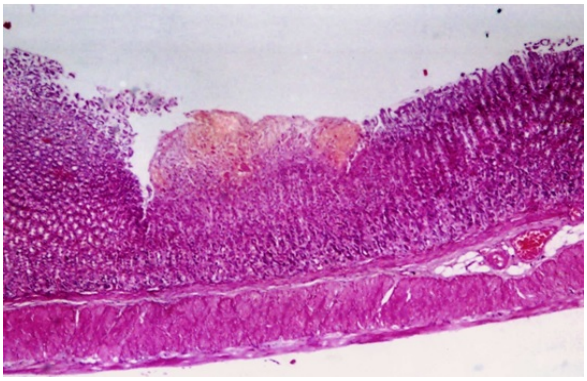

Figure 1A. Histologic appearance of mucosal lesions induced by CRS in rats

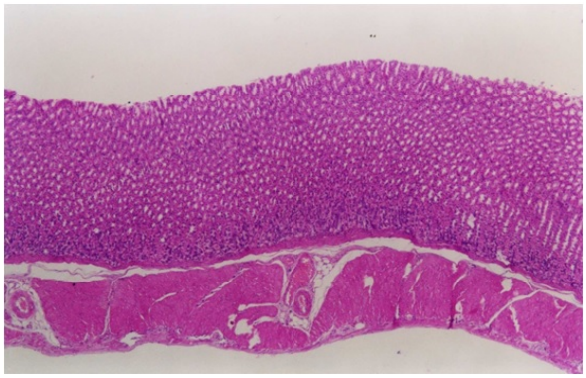

Figure 1B. Pretreatment with PPC significantly reduced gastric mucosal injury induced by CRS

Oxidative stress

Xanthine oxidase is one of the enzymes participated in purine catabolic pathway catalyzing the conversion of hypoxanthine to uric

acid with release of the superoxide radical as by-product. The other radical producing mechanism is nitric oxide

(NO). Our studies indicate that stress significantly increased the production of

ROS such as XO and nitrate+nitrite in the gastric tissue (p< 0.00) (Table 2). PPC pretreatment significantly inhibited the generation of these ROS in the group C rats (p< 0.00) (Table2).

Anti-oxidant enzymes activity and lipid peroxidation

Superoxide dismutase, and catalase activity are induced by the level of their individual reactive species, i.e., superoxide anion and hydrogen peroxide, respectively, the reduced level of superoxide anion and hydrogen peroxide may lead to decreases in the activity of superoxide dismutase and catalase. SOD dismutase O_2^- into H_2O which is scavenged by peroxidase and catalase. Our results indicated that stress significantly decreased the anti-oxidant enzyme activities namely SOD (p<0.001) and erythrocyte CAT (p< 0.00) (Table 2), In the PPC pretreatment group, SOD (p<0.001) and CAT (p<0.001) activities significantly higher than the CRS rats. It is known that GSH is the predominant thiol of a tissue in normal animals. Thus, the decrease in tissue thiol levels may reflect the oxidation or degradation of GSH, or both. As shown in Table 2, gastric GSH decreased significantly during CRS. PPC pretreatment effectively prevented the decreasing in gastric GSHlevels.

MDA level as a metabolic product of lipid peroxide was significantly higher in CRS group than control and PPC+CRS groups. Pretreatment with PPC significantly lowered the MDA levels (p<.001). PPC treatment significantly inhibited the CRS induced lipid peroxidation in gastric tissue. These results showed to PPC as a potent antioxidant effect (Table 2).

Evaluation of mast cell degranulation

Mast cells from different locations are shown to vary different properties such as histochemical, ultrastructural, cytochemical, and functional properties. Depending on their heterogeneity, they are categorized as mucosal (MMC) and connective tissue (CTMC), which are also called atypical and typical mast cells, respectively. Differences in the charge distribution of the proteoglycan matrix of mast cells may also be revealed by staining with combinations of dyes such as alcian-blue and safranin. Connective tissue mast cells can be stained alcian-blue and safranin red to blue according to their heparin content. When heparin synthesis increases, cells stainonly safranin (red-stained) and in case of a decrease in heparin synthesis cells stain only alcian blue (blue-stained). Mucosal mast cells, containing little or no heparin, are stained only alcian-blue. In the present study, stress induced degranulation of both red and mix stained mast cells in submucosal and muscularis propria layer of the gastric wall in group 2 rats (Figure 2A). However, PPC pretreatment significantly inhibited red and mix-stained mast cell degranulation in both layer of gastric wall. (p < 0.001) (Figure 2B, Table 1).

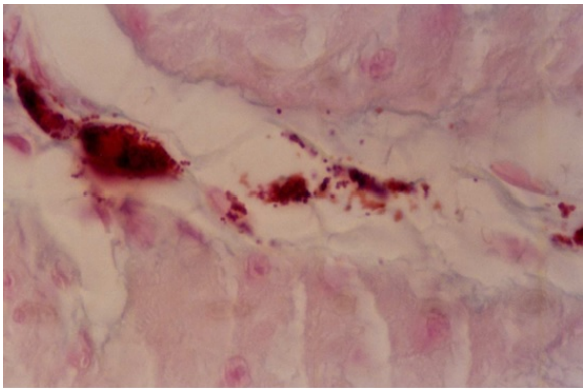

Figure 2A. Stress induced mast cells degranulation (red stained) in submucosal layer of gastric tissue in group 2 rat. (Alcian blue-safranin X 1000)

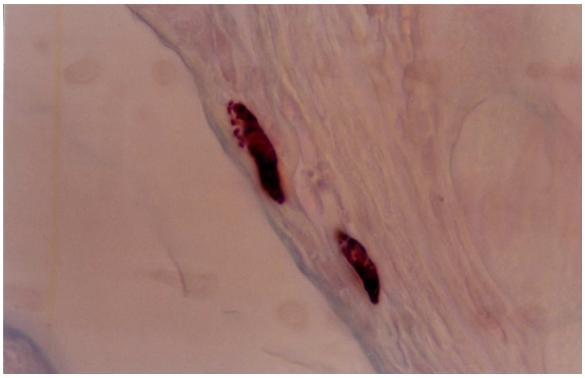

Figure 2B. PPC pretreatment significantly inhibited mast cell degranulation (red stained) submucosal and muscular layers of gastric tissue in group 3 rat. (Alcian blue safranin X 1000)

Plasma PGE_2 and LTC_4 levels

As prostaglandin plays an important role in cytoprotection of gastric mucosa include various damaging factors, it is interesting to investigate the effect of stress on the PGE_2 levels. PGE_2 decreased during cold restraint stress. PPC pretreatment significantly prevented the depletion of PGE_2level. The mean PGE_2level was remaining to be 201.1±35.2 pg/ml in PPC pretreated group ($p<0.001$)(Table 2). LTC_4 is an offensive factor to development of stress ulcer. As shown in Table 2, CRS produced significantly increase in plasma LTC_4 level as compared to control rats ($p<0.001$). Administration of PPC partly but significantly prevented these increase as compared to non-treated group (27.8±6.1 pg/ml and 62.9±4.8 pg/ml, respectively,$p<0.001$).

DISCUSSION

Results of our experiment shows that the production of the gastric mucosal lesions by CRS which associated with the degranulation of mast cells, generation of ROS, decrease of anti-oxidant enzyme levels, decrease of PGE_2 levels, as well as increase of LTC_4 levels. The present works also demonstrates that PPC pretreatment markedly decreased CRS-induced gastric mucosal injury. Histopathologic and laboratory analysis revealed that PPC pretreatment effectively inhibited CRS-induced mast cell degranulation. PPC pretreatment also resulted with an increase in PGE_2 synthesis and a decrease in LTC_4 production in CRS rats.

Mast cells can participate in many biological responses such as allergic disease, acute and chronic inflammatory disorders, fibrotic conditions, wound healing, tissue remodeling, and host responses to parasites and neoplasm. Mast cell granules contain many potent mediators, such as histamine, heparin, proteases, leukotrienes and a broad spectrum of multifunctional cytokines (19-20). Stomach mast cell degranulation has been shown to be important in the pathogenesis of stress induced gastric ulcer formation; recent findings suggest that anti-ulcer effect of vasoactive intestinal peptid and ethacrynic acid could be due to inhibition of degranulation of these cells. Recently, this suggestion is supported by several authors. Khadzhiev et al (21) reported that stress induced gastric ulcers revealed marked circulatory disturbances in ulcerated gastric mucosa which include with arteriolar spasm and leading to perivascular edema, diapedesis of erythrocytes, and micro hemorrhages. They observed that arteriolar spasm and subsequent hypoxia promote the release and activation of inflammatory mediators such as histamine, serotonin, leukotriens, cytokines, proteoglycans and platelet-activating factor. These changes were most pronounced on day one after stress and progressively decreased with ulcer healing. The granules of mast cells are the main source of histamine, serotonin and other mediators (21). Thus, it has been thought that, certainly, degranulation of mast cell plays a very important role in the pathogenesis of stress ulcer through inflammatory mediators and neurohormonal regulation of the microvascular tone (21). In the present study, PPC pretreatment effectively inhibited the stress induced degranulation of red and mix– stained mastcell.

It has been shown that rats feeding on different dietary fats have major changes in the fatty acid

composition of membrane phospholipids of their mast cells. Changes were predominantly observed in polyunsaturated fatty acids of (n-6) and (n-3) families, which could be explained by the metabolic fate of these particular fatty acids of these families. Alterations in the content of polyunsaturated fatty acids in membrane phospholipids may lead to changes in membrane fluidity which influences membrane fusion processes and the microenvironment of receptors. Consequently, it may reasonable to presume that differences in membrane fluidity might influence the release of substances stored in the granules. Our results clearly show that PPC pretreatment and consequent changes in plasma fatty acid composition resulted with mast cell stabilization and/or inhibition of mast cell degranulation in CRS rats. Further investigation is required to elucidate the exact mechanism for explain the influence of PPC on mast cell membrane fluidity and/or stability.

It has been implicated that oxygen free radicals and lipid peroxidation induced via these radicals play in important role in the pathogenesis of stress-induced gastric mucosal injury in experimental animals and humans as well. It was concluded that free radical might thus be one of the factors involved in the pathogenesis of gastric mucosal lesions induced by CRS.[4] The CRS may cause ischemia-reperfusions in the gastric mucosa by microcirculation disturbance with links to further chain. Lipid peroxidation may also be involved in this process, causing damage in gastric mucosa as seen in various stress ulcer models. [22] Some authorshave been demonstrated that the changes of gastric mucosal active oxygen metabolism and blood flow are closely related to the formation, progression, and recovery of gastric mucosal lesions in rats with a single injections of compound48/80,amastcelldegranulator.Inadditi on,theyshowedthat48/80inducedgastric mucosal injury could be a kind of ischemia-reperfusion induced-injury occurring through degranulation of connective tissue mast cell. Recently, this suggestion is supported by several authors. Study our findings confirmed that there was a close relationship between the mast cell degranulation and oxidative mucosal injury in CRS rats. Accordingly, it is conceivable that PPC pretreatment protects againts acute mucosal lesions in CRS rats by protecting the gastric mucosal tissue from the attack of ROS derived from the xanthine-XO system and/or lipid peroxidation mediated by ROS through an indirect antioxidant action depending on its preventive effect of mast cell degranulation. In addition, both in vitro and in-vivo studies revealed that PPC, and its main component dilinoleoylphosphatidylcholine (DLPC), have strong anti-oxidant and cytoprotective effects. It don't yet fully understand the mechanism(s) of this anti-oxidant action of DLPC, it was suggested that high bioavailability and great capacity for incorporation into the membranes (damaged by oxidative stress), it could play a role in the repair of these membranes. It also has been shown DLPC could provide a "trap" for the free radicals. The combined effect of these unusual properties of PPC may account for antioxidant effects against experimentally induced stressulcer (23).

Prostaglandin E_2 and prostacyclin (PGI_2) inhibit histamine and vagal-stimulated gastric acid secretion and potent vasodilators increasing gastric mucosal blood flow. Arachidonic acid also inhibits gastric acid secretion. Leukotrienes, however, promote inflammation and retard the healing of ulcers. Ulcer formation can be associated with a relative change in the amounts of these products of arachidonic acid oxidation (24-25). Accordingly, it has been thought that arachidonic acid is slide from cyclooxygenase pathway to lipoxygenase pathway by CRS. Pretreatment with PPC resulted with high plasma arachiodanate levels and turned inside out this event, and PGE_2 level increased and LTC_4 level

decreased. Inhibition of mast cell degranulation also account for decreased LTC_4 levels in PPC pretreatedrats.

Table 1. Mast cell heterogeneity and mast cell degranulation levels of groups

	Red stained mast cells		Mixt stained mast cell		Blue stained mast cells	
	Granulated	Degranulated	Granulated	Degranulated	Granulated	Degranulate
Control	25.9±5.2	0.53±0.2	0.86±0.2	0.03±0.001	0.13±0.006	0.003±0.001
CRS	33.6±5.07	4.4±0.7	0.73±0.18	0.002±0.01	0.31±0.13	0.0±0.0
PPC+CRS	27.1±3.5	1.22±0.27*	0.53±0.30	0.004±0.001	0.1±0.1	0.0±0.0

*P < .001 compared with group CRS rats

Table 2. Effects of PPC Pretreatment on histopathological and biochemical results of CRS-Induced Gastric Damage

Groups	Gastric lesions		Antioxidant enzyme activities			Oxidant levels		Lipid peroxydation	Eicosanoids	
	UI (mm)	Inhibition percentage (%)	CAT (k/g protein)	SOD (u/mg protein)	GSH (µmol/gwet tissue)	XO (u/g prot)	Nitrit+nitrat (µmol/L)	MDA (mmol/g wet tissue)	PGE_2 (pg/ml)	LTC_4 (pg/ml)
Control	-	-	367.8±85.2	48.5±5.4	5.2±1.02	1.6±0.07	22.5±2.5	5.1±0.96	232.5±67.3	23.1±6.9
CRS	23.6±4.1	-	119.5±32.3	25.04±2.4	1.38±0.4	2.4±0.3	53.5±7.1	26.01±5.6	86.2±15.2	62.9±4.8
PPC+CRS	0.8±1.3*	96.4*	248.1±46.3*	37.4±3.8*	2.8±0.4*	2.06±0.1*	32.5±3.5*	9.69±1*	201.1±35.2*	27.8±6.1*

*P < .001 compared with group CRS rats

Table 3. Fatty-acid composition of groups

Fatty-acid	Control	Control+PPC	CRS	PPC+s-CRS
Palmitic acid (16:0)	17,43±0,66	19,30±1,27	28,80±3,99	28,62±4,11
Stearic acid (18:0)	24,22±1,08	21,53±2,17	20,48±3,18	22,68±3,16
Oleic acid (18:1)	10,70±1,19	10,16±1,57	19,91±3,48	23,38±3,87
Linoleic acid (18:2)	16,10±0,48	14,32±1,07	16,83±4,04	17,37±3,60
AA (20:4)	15,12±0,48*	16,67±0,71*	9,97±3,13	15,44±0,68*
DHA (22:6)	8,02±0,66	_	3,73±3,97	2,08±3,41

Abservations : AA, arachidonic acid; DHA, docosahexaenoic acid,

*p < 0.001; Compared to CRS group.

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