Original Research Article

INFLUENCE OF LYCOPENE ON RENAL TISSUE INJURY IN CELEBREX INDUCED ALBINO RATS; AN EXPERIMENTAL RESEARCH STUDY.

ABSTRACT

Objective: To analyze the renal tissue injury in Celebrex induced albino rats with improvement by lycopene.

Study design: Experimental research study.

Abode of study: Animal House, Basic medical sciences institute, Karachi,

Materials and Methods:

Celebrex and antioxidant agent lycopene were used in this experimental study. Drugs were administered orally to forty male albino rats weighing of around 250gm for research. Rats were retained in isolated cages and alienated into 4 sets including control, diseased, treated groups. The drugs were administered by gastric tube once24-hourly for four weeks. After finalization of research work, rats were sacrificed and body tissues were preserved for staining.

Results: gB Gomori's calcium phosphate stained sections showed marked deposition of dark black particles of alkaline phosphate in cellular cytoplasm of proximal convoluted tubules but gC showed scarce deposition of black particles of alkaline phosphate in the cellular cytoplasm of proximal convoluted tubules.

Conclusion: This experiment discloses that lycopene recuperate the raised level of alkaline phosphate in the cytoplasm of proximal convoluted tubules.

Key words: proximal convoluted tubules, Gomori's calcium phosphate, alkaline phosphate, PGE_2.

INTRODUCTION:

NSAIDs are the number one most frequently recommended medicine & COX enzyme inhibitor for various ailments like inflammation, fever, arthritis and painful illnesses. They further categorize on the basis of (COX) enzyme selectivity. One group inhibits both COX 1 & 2 whereas second group is only cox-2 inhibitor.[1] Non-selective group raise the risk of gastric ulcers and intestinal bleeding due to weakening of prostaglandin-dependent mucosal protective ability because NSAIDs inhibits prostaglandins synthesis[2,3]. PGE_2 regulates the fluid metabolism and hemodynamic in renal tissue and its inhibition plays a significant role in inflammation, peptic ulcer ailment, renal dysfunction and impairment of intestinal mucosa[4]. Myeloperoxidase enzyme (MPO) found in neutrophils and macrophages plays an important role in inflammation and oxidative stress.[5,6] Organs in which Xenobiotic metabolism occur are kidney, liver & GIT. It is the type of metabolism in which biochemical alteration of drug take place by enzymes. Celebrex is COX-2 enzyme inhibitor & COX-2 enzyme mainly affect salt and water excretion, so it has toxic effect on kidney. It can cause cellular injuries & degenerative changes in renal tissue such as chronic renal failure, nephropathy & interstitial nephritis[7]. Acute renal injury is described by accumulation of urea, alkaline phosphatase & creatinine in plasma[8]. Alkaline phosphatases are present in proximal convoluted tubules of renal tissue & altered due to nephrotoxic drugs[9]. Celebrex a selective COX-2 inhibitor has GI tolerability & has a reduced amount of bowel injury[10,11,12]. Usage of cox2 inhibitors causes renal tissue injury & elevates serum alkaline phosphatase in end stage renal disease patients, which causes reduced BP, kidney calculus

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gastrointestinal

formation, angina pectoris, shortness of breath, deafness, Mediterranean illness cardiovascular ailments, atherosclerosis & death[13,14] ~~13,14~~.

Lycopene is a red carotenoid phytochemical noncyclic complex present in apricots, asparagus, parsley & other vegetables. It prevents lipid per oxidation & undergo oxidative, thermal and photo degradation[15,16] ~~15,16~~. Lycopene ~~F~~found in blood plasma anti-carcinogenic, anti-inflammatory and antioxidant in character. Inhibits prostaglandin synthesis & also prevents various malignancies, Alzheimer's ailment, & cardiovascular illnesses, as well as reduces ageing[17] ~~17~~. It prevents cellular damage due to scavenging properties of reactive oxygen species, singlet oxygen-quenching capability, several conjugated double bonds & reacts with reactive oxygen species to decrease DNA mutilation[18,19,20] ~~18,19,20~~. It also prevents lipid ~~peroxidation~~per oxidation in cellular basement membrane[21,22,23] ~~21,22,23~~. It detoxifies toxins by antioxidation, anti-inflammation activitiy[24,25] ~~24,25~~. The experimental research study was organized to examine the advantageous effects of lycopene in comparison with injurious effects of Celebrex.

MATERIAL AND METHODS

This is a 4 weeks experimental research study, came about in JPMC, Karachi along with endorsement from ethical review board No.F-1-2/BMSI-E.COMT/039/JPMC. 40 fully grown up healthy albino rats, three to four months old, around 250gm were taken from USA lab and fostered in animal house in isolated cages. Assessed for 7 days for their health condition and weighed former the beginning of research and isolated into 4 sets (control, diseased, treated) and dosage calculated according to their weight. Tablet Celebrex purchased from Getz Pharma & lycopene pigment capsule from General Nutrition Corporation, [26,27] were

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administered by gastric tube 0.05g/kg orally once24-hourly for four weeks. After finalization of research work, rats were sacrificed and body tissues were preserved for staining.

gA= control.

gB=: Celebrex 0.05g/kg per oral. (Morbid group)

gC= Celebrex with lycopene pigment 0.05g/kg per oral.

gD= lycopene pigment 0.05g/kg per oral.

Throughout the experimental duration animals were deeply observed for variance in their conditions. They were sedated by ethanol and fixed on a dissecting panel. A vertical cut was given from sternum to pubic bone. Renal tissue was washed with saline water and fixed in 10 % ~~ten percent~~ formalin for 24 hours, then kept for dehydration in 70% alcohol overnight. Further dehydrated by ascending concentrations of alcohol, after that cleared in xylene. Paraffin infiltration take place at 58 ^{0}C in lab oven and paraffin blocks prepared. 4 micron dense slices were excised on microtome & placed in warm H_2O bath at 40 ^{0}C and fixed on albumenized glass slides at 30 – 32 ^{0}C. Gomori's calcium phosphate was used to observe alkaline phosphatase activity in proximal convoluted tubular cells (8X ocular and 40X objective lens)[28] ~~[28]~~.

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RESULTS

Microscopic observation of Renal Tissue with the help of Gomori's calcium phosphate staining

gA:

Gomori's calcium phosphate stained renal sections of gA showed less or no black particles of alkaline phosphate in the apical area of cellular cytoplasm. (Figure-1).

gB:

Gomori's calcium phosphate stained kidney sections showed marked deposition of dark black particles of alkaline phosphate in cellular cytoplasm of proximal convoluted tubules (Figure-2).

gC:

Gomori's calcium phosphate stained section of this group showed rare deposition of black particles of alkaline phosphate in the cellular cytoplasm (Figure-3).

gD:

Gomori's calcium phosphate stained section of this group showed rare or no black particles of alkaline phosphate in the apical area of cellular cytoplasm just like gA.

Figure-1

Gomori's Calcium Phosphate stained, 4 µm thick section of control albino rat kidney showing less amount of Alkaline Phosphate particles (ALP) in Proximal tubule (Photomicrograph x 400)

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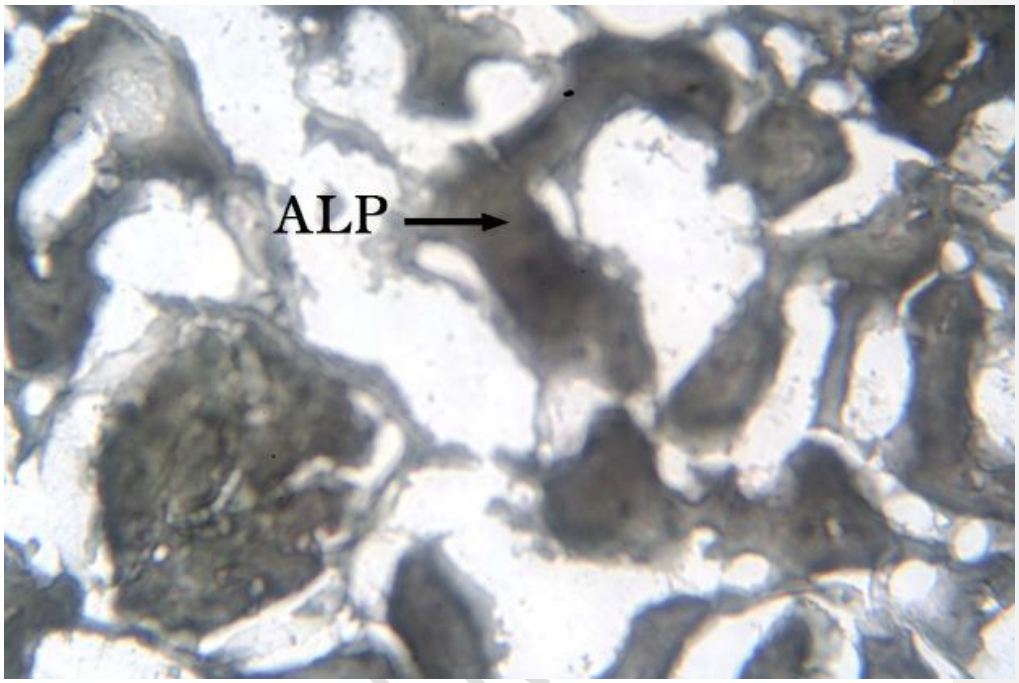

Figure-2

Gomori's Calcium Phosphate stained, 4 µm thick section of control albino rat kidney showing grayish black Alkaline Phosphate particles (ALP) in Proximal tubule of Celecoxib treated group. (Photomicrograph x 400)

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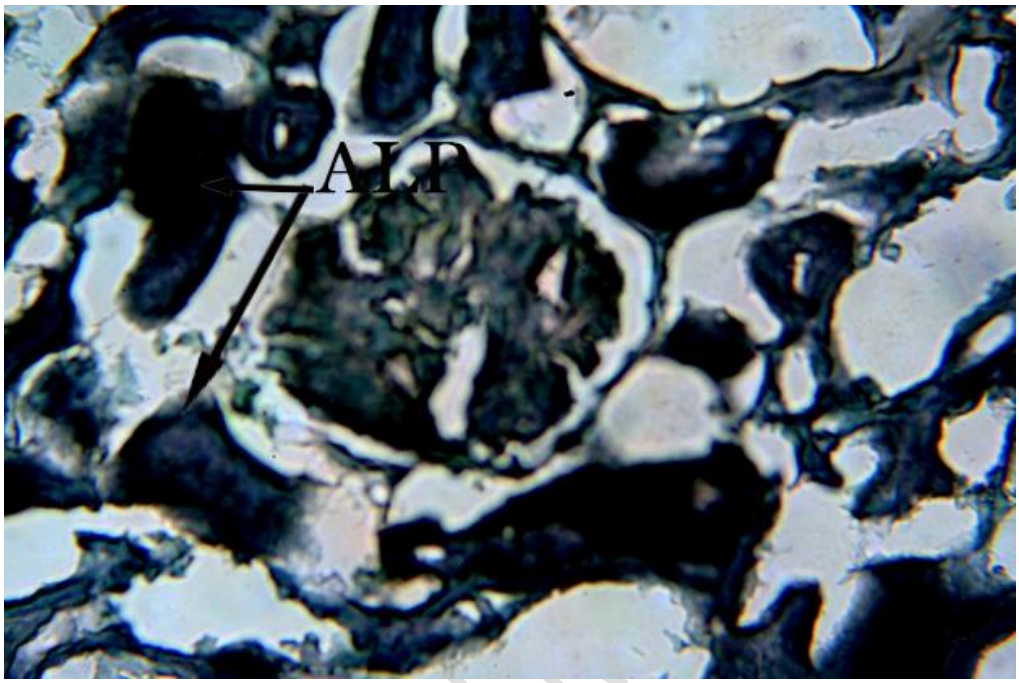

Figure-3

Gomori's Calcium Phosphate stained, 4 µm thick section of albino rat kidney showing few Alkaline Phosphate particles (ALP) in Proximal tubule of Celecoxib + Lycopene treated group. (Photomicrograph x 400)

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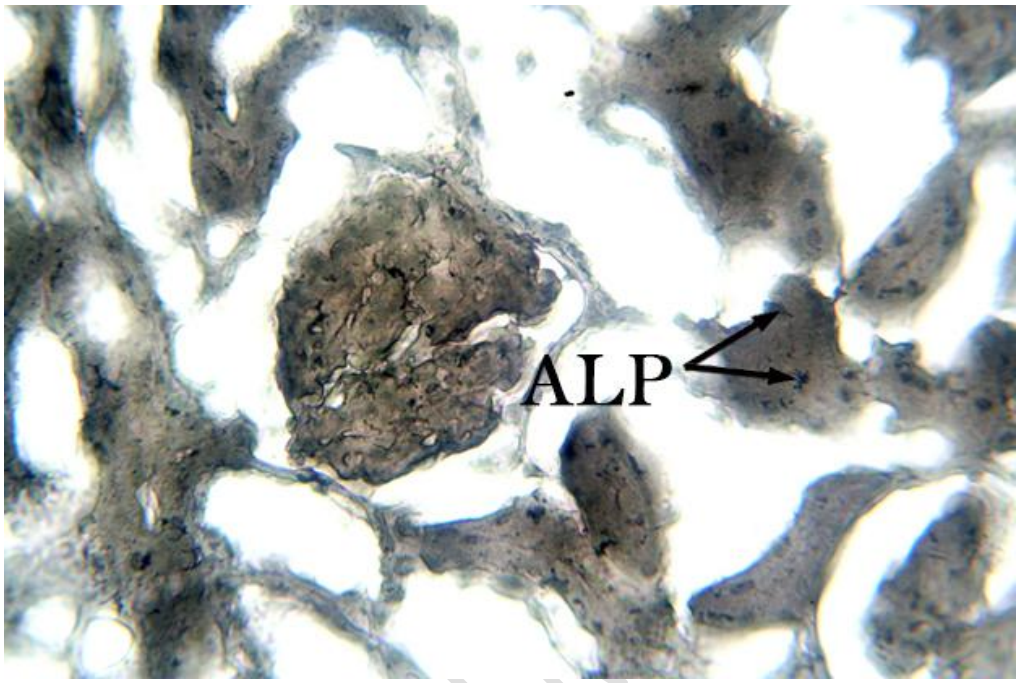

DISCUSSION:

NSAIDs administration is hazardous for nephropathy & causes inflammation by inhibiting COX enzyme develops renal injury. It blocks prostaglandins synthesis necessary for renal ischemia, renal perfusion & renin discharge[1,2]. ~~[1,2]~~ It is associated with various harmful effects like Peptic ulcers, dyspepsia, edema and retention of electrolytes[5] ~~[5]~~.

Lycopene is a red carotenoid antioxidant phytochemical noncyclic complex found in apricots, asparagus, parsley & other vegetables. Prevents lipid per oxidation & undergo oxidative, thermal and photo degradation, CNS injury, hepatic damage, renal damage, act as an anti apoptotic mediator[15,16] ~~[15,16]~~. Lycopene ~~F~~found in blood plasma anti-carcinogenic, anti-inflammatory and antioxidant in character. Inhibits prostaglandin synthesis & also prevents various malignancies, Alzheimer's ailment, & cardiovascular illnesses, as well as reduces ageing[17] ~~[17]~~.

Gomori's calcium phosphate stained kidney sections of gB showed marked accumulation of dark black particles of alkaline phosphate in cellular cytoplasm of proximal convoluted tubules Similar results were also explained by[9,13] who said that numerous nephrotoxins injured proximal convoluted tubules by varying alkaline phosphatase action & raised levels are closely related with renal ailment & death of patients.

Gomori's calcium phosphate stained section of gC showed rare deposition of black particles of alkaline phosphate in the cellular cytoplasm at apical surface of proximal convoluted renal tubules. Similar results were also explained by[15,25] who determined that amendment & reversal of harmful effects in serum levels of alkaline phosphatase occur with administration of lycopene due to its potent antioxidant properties.

CONCLUSION:

This experimental research study concluded that gB rats had marked accumulation of dark black particles of alkaline phosphate in cellular cytoplasm of proximal convoluted tubules due to renal injury on the other hand gC animals presented with rare deposition of black particles of alkaline phosphate in the cellular cytoplasm. Thus our hypothesis from this experimental work is that celebrex is injurious for kidneys & other vital organs while lycopene is advantageous for health because of its anti-oxidative properties.

LIMITATION OF STUDY

~~we~~ We have insufficient funds to do it in more depth.

ETHICAL APPROVAL

Anatomy department of BMSI gave us ethical approval (Ethical review board No.F-1-2/BMSI-E.COMT/039/JPMC).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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