ORIGINAL ARTICLE

Prophylactic Role of Curcumin against Presence of Mononuclear Cell Infiltrates in the Interstitium of Kidneys caused by Aspirin in Adult Female Albino Rats

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ABSTRACT

Background: The most frequently used non-steroidal anti-inflammatory drug worldwide to treat pain, inflammation and fever is Aspirin.Curcumin frequently referred to as "Haldi" is a chemical constituent of turmeric powder that is utilized in Ayurvedic medicine.
Aim: To evaluate the nephroprotective effects of curcumin against the presence of mononuclear cell infiltrates caused by aspirin within the interstitium of kidneys in adult female albino rats.
Study design: Experimental study.
Methods: 15 rats were distributed in each of the 4 groups and study was conducted for 30 days. Aspirin (200 mg/kg bodyweight) was given to rats by orogastric intubation to induce nephrotoxicity in positive control group B and experimental groups C & D. Moreover, the rats of experimental groups C &D in addition to aspirin received 15 mg/kg &30 mg/kg body weight of curcumin by orogastric intubation.
Results: On histopathological examination, the mononuclear cell infiltrates werenot observed in control group A. However, the infiltrates were seen in all rats of positive control group B and 6 (40.0%)&4 (26.7%) ratsin experimental groups C &D respectively. This difference was found significant with p-value 0.002.
Conclusion: The present study has depicted that curcumin reduces the inflammation by decreasing the mononuclear cell infiltrates in the interstitium of kidney and the outcomes are dose dependent.
Keywords: Aspirin, Curcumin, Mononuclear cell infiltrates, Interstitium, kidneys, adult female albino rats

INTRODUCTION

Aspirin is commonly used as an effective pain reliever and fever reducing agent,worldwide. It produces toxicity of kidney by inhibiting synthesis of prostaglandin[1]. It suppresses the production of prostaglandins and thromboxanes due to irreversible inactivation of the cyclooxygenase[2]. Aspirin is used as one of the most cheap, famous and easily available drug. It causes vasoconstriction and atrophy of smooth muscles in kidneys by inhibition of prostaglandins[3].

Prostaglandin inhibitionhas a profound effect on blood flow to the kidneys and glomerular filtration rate[4]. Studies have shown that sexually mature female rats are more susceptible to aspirin induced nephrotoxicity than male and immature female rats[5]. This is because of the fact that females have low levels of serum aspirin esterase levels that degrade aspirin more slowly thus, producing more nephrotoxicity[6]. Aspirin has many therapeutic uses in various ailments. It helps to reduce the risk of cardiovascular diseases, Alzheimer's disease and prevention of colorectal cancer[7]. It decreases the progression of atherosclerosis. Aspirin induced inhibition of cyclooxygenase results in loss of cytoprotective effects of prostaglandins on gastric mucosa resulting gastrointestinal disturbances. Aspirin is contraindicated in patients with peptic ulcer disease, gastrointestinal bleeding, alcoholism, and intracranial hemorrhage[8].

Curcumin is a polyphenol obtained from the rhizome of the plant Curcuma Longa, commonly known as turmeric[9]. Turmeric belongs to ginger family[10]. It is used as a spice and a food flavouring product[11] & being extensively cultivated in tropical and sub-tropical areas of the world[12]. The curcuminoids that are derived from turmeric are: 71.5% Diferuloylmethane, 19.4% demethoxycurcumin and 9.1% bisdemethoxycurcumin[13,14]. It also contains volatile oils, proteins,sugars, and resins.The curcuminoids are also called as "INDIAN SAFFRON"[15]. Curcumin possessesanti-inflammatory, anti-atherosclerotic[15], antioxidant, antispasmodic, anti-bacterial, anti-human immune-deficiency virus, anti-protozoal and nematocidal actions[12]. The beneficial effects of curcumin against swelling and sprain injurieswere alsowell established.[17]Curcumin promotes wound healing; inhibits formation of gall stone; prevents septic shock, cardiovascular diseases, inflammatory bowel disease; hepatotoxicity & nephrotoxicity[18] and arthritis[19]. It inhibits generation of free radicals and lipid peroxidation and protects DNA from oxidative damage[20]. It inhibits structural damage by lowering glomerulosclerosis Index (GI), interstitial fibrosis and arteriolopathy[21]. Curcumin down regulates the activity of drug metabolizing enzymes cytochrome P450 that results in toxicity of some drugs[22]. Various facts indicate

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that curcumin acts as a bifunctional antioxidant and exerts both direct and indirect antioxidant effects[23].

Curcumin is frequently used as a food additive therefore, the present study was designed to evaluate the prophylactic effects of curcumin against the presence of mononuclear cell infiltrates in the interstitium caused by aspirin in adult female albino rats.

MATERIAL AND METHODS

This experimental study was performed in the Department of Anatomy, Shaikh Zayed Postgraduate Medical Institute, Lahore. All rats were kept in cages in the animal house of the Department of Anatomy, PGMI, Lahore. The rats were allowed free access to food and water.A 12 hourly light : dark cycle was maintained at room temperature of 27°C. After acclimatization for 15 days, these rats had been kept in separate cages divided into 4 groups A, B, C and D with appropriate labeling. 15 rats were allocated in each group. Body weight was measured before and after the experiment. Blood samples had been taken from the rat's tail before the experiment and then on 15th and 30th day of experiment, for creatinine assay of all four groups. A lignocaine cream as a local anaesthetic was applied to the site 30 minutes prior to blood sampling.[24]

Turmeric extract was prepared from PCSIR laboratory, Lahore. Quantification of extract was done through Gas Chromatography-Mass Spectrometry (GC-MS) from Chemistry Department of Forman Christian College, Lahore. Turmeric extract had been given to the rats through orogastric intubation. All the groups had 15 female wistar rats.

Group A (Healthy Control Group): Received 10ml/kg body weight/day of distilled water.

Group B (Positive Control Group): Received 100mg/kg body weight/day of aspirin for 30 days.

Group C (Experimental Group I): Received100mg/kg body weight/day of aspirin and 15mg/kg body weight of curcumin simultaneously for 30 days.

Group D (Experimental GroupII): Received100mg/kg body weight/day of aspirin and 30mg/kg body weight of curcumin simultaneously for 30 days.

After dissection, the kidneys had been removed and studied histologically for the presence of mononuclear cell infiltrates.

Statistical Analysis: Data was entered and analyzed by using SPSS 22.0. The qualitative data for the presence of mononuclear cell infiltrates was reported by using frequency and percentage of each group. Comparison among groups was made by using Chi-square test. P-value ≤ 0.05 was considered significant.

RESULTS

The interstitium of kidney appeared normal in control group A (Fig.1) while mononuclear cell infiltrates wereobserved in all rats of positive control group B and 6 (40.0%)& 4 rats (26.7%) in experimental groups C &D respectively. (Fig.2, 3 & 4) This difference was found significant with p-value 0.002 (Table.1).

The positive control group B and experimental group C had highly significant difference from experimental group D with p-values <0.001 and 0.017 respectively. The difference between control group A and experimental group D was insignificant with p-value 0.100. The experimental groups C and D both had significantly less number of rats with mononuclear cell infiltratesin the interstitium as comparedto positive control group B with p-values 0.001 and <0.001. The experimental group D and experimental group C had insignificant difference with p-value 0.699. (Table. 2 & Fig.5)

Fig.1: Photomicrograph of kidney of adult albino rat of control group A showing: Glomerulus (G), Proximal convoluted tubule (PCT), Distal convoluted tubule (DCT) and Blood vessel (BV). (H&E, 10x)

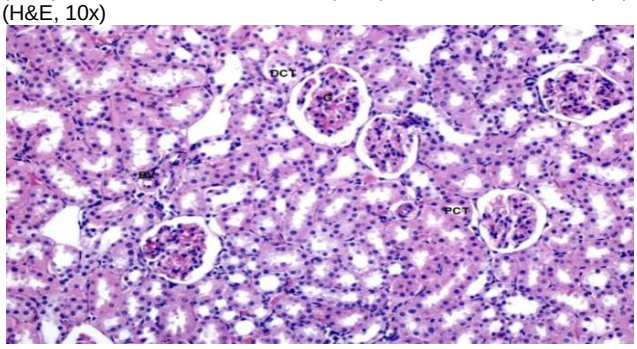

Fig.2: Photomicrograph of kidney of adult albino rat of positive control group B showing: Proximal convoluted tubule (PCT), Distal convoluted tubule (DCT) and more mononuclear cell infiltrates (yellow arrow) in the interstitium. (H&E,10x)

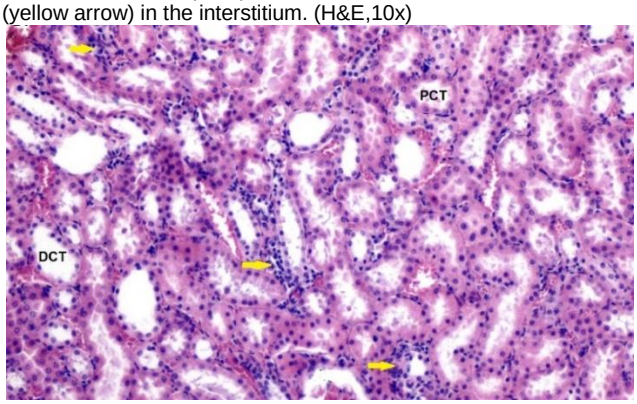

Fig.3: Photomicrograph of kidney of adult albino rat of experimental group C showing: Blood vessel (BV), Proximal convoluted tubule (PCT), Distal convoluted tubule (DCT) and less mononuclear cell infiltrates (yellow arrow) in the interstitium. (H&E,10x)

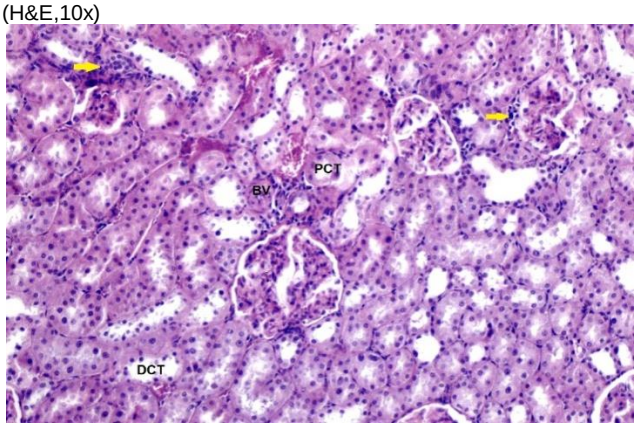

Fig.4:Photomicrograph of kidney of adult albino rat of experimental group D showing: Proximal convoluted tubule (PCT), Distal convoluted tubule (DCT) and less mononuclear cell infiltrates (yellow arrow) in the interstitium. (H&E,10x)

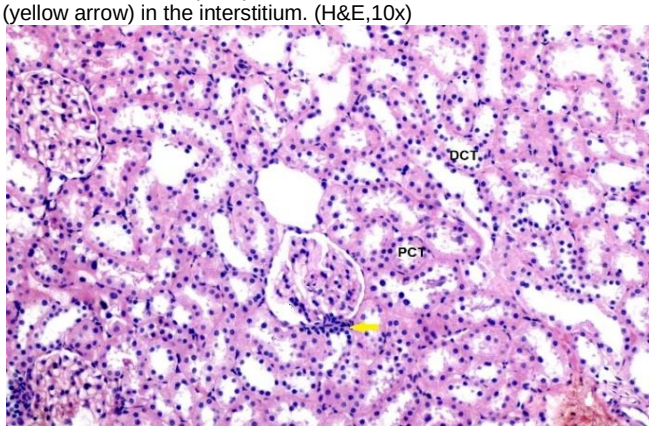

Fig.5: Graphic comparison of presence of mononuclear cell infiltrates among control groups given aspirin and experimental groups given aspirin & curcumin

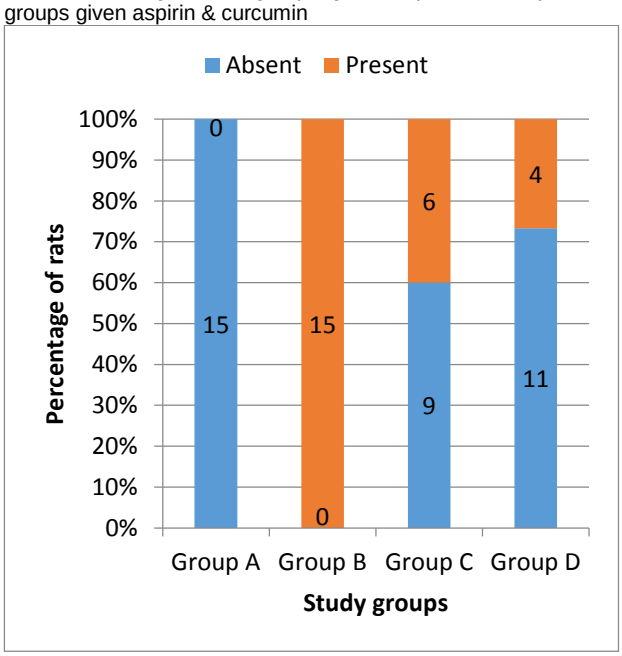

Table 1: Comparison of the presence of mononuclear cell infiltratesamong control groups given aspirin and experimental groups given aspirin & curcumin

Group	Mononuclear Cell Infiltrates		
	Present	Absent	Total
A	0	15(100%)	15(100%)
B	15(100%)	0	15(100%)
C	6(40%)	9(60%)	15(100%)
D	4(26.7%)	11(73.3%)	15(100%)

Chi-square = 33.12 p-value = 0.002

Table 2: Group wise comparison of presence of mononuclear cell infiltratesamong control groups given aspirin and experimental groups given aspirin & curcumin (by using chi-square)

(I) Group	(J) Group	Chi-square	Df	P-value
A	B	26.13	1	<0.001**
	C	5.21	1	0.017*
	D	2.60	1	0.100+
B	C	10.16	1	0.001*
	D	14.35	1	<0.001**
C	D	0.15	1	0.699+

KEY

A: Control Group of rats
B: Positive control Group of rats
C: Experimental Group I of rats
D: Experimental Group II of rats
N: Number of rats in each group
Df: Degrees of freedom
**Highly significant difference (P<0.001)
*Significant difference (P<0.05)
+Insignificant difference (P>0.05)

DISCUSSION

Aspirin has been employed as one of the most economical and readily available non-steroidal anti-inflammatory drug. It exhibitsversatileanti-inflammatory; anti-platelet; anti-pyretic & analgesic properties. It also has a beneficial role in joint diseases[3,8]Curcumin is a food additive and a pigment commonly used in foods in Asia[25].

In the present research work the mononuclear cell infiltrates were observed in more rats in positive control group B followed by experimental groups C & D. (Fig.2, 3 & 4)This difference among groups were significant with p-value 0.002. (Table.1)These observations are consistent with the results of previous study which revealed the presence of interstitial infiltrates particularly lymphocytes with vacuolar degeneration of the proximal and distal convoluted tubules[26]. The possible role of aspirin producing mononuclear cell infiltration is caused by a decrease in the antioxidant level and the increased oxidative stress due to the overproduction of ROS. This initiates an inflammatory response cascade leading to irreversible tissue damage[27]. The decreased mononuclear cell infiltrateswere observed in experimental groups C & D given curcumin. The inhibitory effect of curcumin on inflammatory cytokines is due to the reduction of the NF-κB signaling pathway. Curcumin has a free radical scavenger properties. It significantly improves immunoglobulins levels and mRNA expression. Curcumin downregulates the expression ofTGF-β1 by decreasing the degree of inflammation thereby, reducing interstitial infiltrates[28].

CONCLUSION

The results of the present study concluded that the co-treatment of aspirin with the ethanolic extract of turmeric prevented aggregation of mononuclear cell infiltrates in the interstitium of kidneys caused by aspirin in adult female albino rats.

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