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IMPACT OF PHENOLIC COMPOUNDS ON CHRONIC KIDNEY DISEASE

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Abstract:
Phenolic compounds are exist in water bodies due to discharge of polluted waste waters from industrial and agricultural are known to be toxic and both humans and animals. One of the phenolic derivative is Bisphenol A (BPA) which is mainly found in plastics, epoxy resins. These are harmful to kidney, endocrine system & reproductive system. The detrimental renal eff ects attributed to phenol toxicity include tubular necrosis, protein cast formation, and papillary hemorrhage. To the best of our knowledge, there is not a comprehensive study on renal biochemistry and ultrastructural changes of the kidney due to phenol administration. Th e purpose of the present study was to investigate the eff ects of phenol administration on the biochemical and histological integrity of the kidney in BALB/c mice

Keywords: Phenolic compounds, Toxicity, CKD

INTRODUCTION:

Phenoilic compounds are class of organic compounds with a hydroxyl groups directly bounded to one or more aromatic rings .The existence of phenolic compounds in water can be attributed to

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natural and anthropogenic activities. Natural sources of phenolic compounds in water pollutions include decomposition of dead plants and animals in the water. Phenolic compounds present in food like hydroxycinnamic acid derivatives Flavanoids such as black grape , apple, citrus fruits , plums , cherries, mangoes , apricot , tomato& leguminous plants like peas , beans and red wine . Phenols are uremic toxins of intestinal origin formed by bacteria during protein metabolism. Of these molecules, p-cresol is the most studied and has been associated with renal function impairment and vascular damage. One of the phenolic compound is bisphenol A (BPA) found in plastic bottles, epoxy resins, hemodialyzers. BPA is conjugated by glucorinic acid in bowel and liver and excreted in urine as

BPA- glucorinide , and these accumulation causes uremic toxins , are responsible for the loss of renal function. Symptoms like anorexia, vomiting, weakness, sleep disturbances, neuropathy and reproductive development.

MATERIALS:

Chemical – Phenol at concentrations of 80 , 180 & 320 mg/kg

Animal – Rat (weight – 30gms)

Estimation of creatinine, BUN & ALP- Jaff e method, Urease-Berthelot method, Enzymatic method spectrophotometer.

METHODS:

1. Renal dysfunction by phenol in water

Phenolic compounds exist in water bodies due to the discharge of polluted waste water from industrial, domestic and agricultural activities into water bodies. These compounds are severe toxic and long-lasting effects on humans and animals. They cause damage to red blood cells and liver by acting as carcinogens. By interacting these compounds with micro-organisms, inorganic and organic compounds in water may produce substituted compounds or other moieties which may be toxic.

2. Renal dysfunction by phenol in food

Ethanol and nonalcoholic wine compounds, especially polyphenols influence oxidative stress it causes nephrons damage leads to improper functioning of the kidney. Flavonoid of naringenin found in grapefruit, oranges, and tomatoes regulates a protein that decreases growths related to kidney cysts, which can lead to kidney failure.

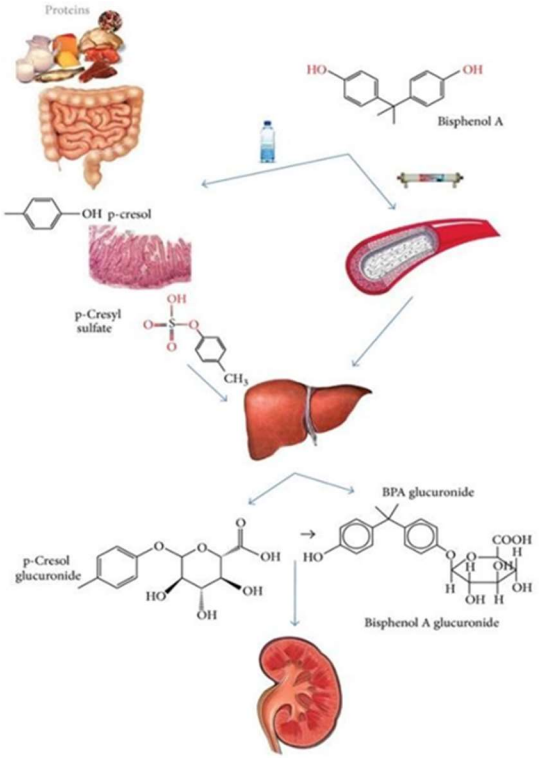
3. Renal dysfunction by BPA in hemodialysers :

Polycarbonate polymers used in several types of medical devices. Industries utilise these for its stability, toughness, optical clarity and resistance to heat and electricity. When BPA is used in medical device products against their efficiency in the treatment, as well as toxicological profile

of alternative materials. Three months of continuous use of same type of dialyser with BPA containing membranes to increase circulating c –reactive protein (CRP) and IL-6 with respective BPA free dialysers .The accumulation of BPA and potential toxicity due to the loss ofBPA excretion mechanism in urine .The migration of BPA from dialysers to the blood of patients and its inefficient removal due to the high protein bound fraction of plasma BPA .

Toxicity of Phenols in ckd

Phenols and indoles are the best-characterized protein-bound uremic toxins. Both have been related to progression of renal failure and to vascular damage. These toxins are metabolites of protein catabolism by intestinal bacteria, which is greatly increased in patients with CKD. Phenols and indoles have been linked to multiple clinical changes in CKD patients. bothindoxyl sulphate as p- cresylsulfate have been associated with accelerated renal function deterioration . BPA is conjugated by glucorinic acid in bowel and liver and excreted in urine as BPA- glucorinide, and these accumulation causes uremic toxins, are responsible for the loss of renal function. Symptoms like anorexia, vomiting, weakness, sleep disturbances, neuropathy and reproductive development.



Procedure:

Experimental design

Th e experiment was carried out for 10 consecutive days and the animals were randomly divided into 1 control group and 3 experimental groups, each comprising 10 mice. Th e control group received only distilled water, whereas the experimental groups received phenol at daily concentrations of 80, 180, and 320 mg/kg, respectively.

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Blood collection

At 24 h aft er administration of the last doses, the animals were anesthetized with chloroform vapor, quickly brought out of the jar. Th ewhole blood was collected into sterilized vials aft er direct cardiac puncture. Blood samples were allowed to clot at 4 °C and centrifuged at 5000 rpm for 10 min. After separation of the sera, they were put intosterile tubes for measurement of the biochemical parameters.

Biochemical analysis

Serum levels of sodium and potassium were measured in advance using flame photometry while levels of chloride and bicarbonate were measured bytitration procedures. Serum samples were analyzed for total protein by the Biuret method, for creatinine(CRT) according to the Jaff e method, for blood ureanitrogen (BUN) by the modified urease-Berthelotmethod, and for alkaline phosphatase (ALP) activity by the enzymatic method, using a spectrophotometer.

Histopathological assessment for renal injury

For optical microscopy, immersion of the left kidney was maintained overnight in 10% neutral buffered formalin for fixation. The kidneys were then sectioned at 5 μm with a microtome and stained with hematoxylin and eosin (H&E). The sections were photographed directly using a stereomicroscopeat 400× high-power fi elds with a Microsoft system. Th e following criteria were used for registeringthe histological changes of the kidney: (++++), adominant change in all of the animals; (+++), are latively common change in all of the animals; (++),a change in all of the animals; and (+), a change in afew of the animals. In each group, 4 samples of renal cortex from each animal were selected and the severities of the lesions were evaluated. According to the changes in the renaltubules, glomeruli, and interstitium, the lesions were classified as mild (+), moderate (++), intense (+++), and severe (++++).

Data analysis and statistics

All of the results were expressed as means and the standard errors of the means. Analysis of variance (ANOVA) was used to test the overall significance of diff erences among the means.

RESULTS:

Effect of phenol administration on the biochemical parameters

The serum levels of sodium, potassium, chloride, bicarbonate, and total protein were not significantly affected, but the CRT, BUN, and activity of ALP in the sera of phenol-treated mice showed a significant increase in comparison with the control group ($P < 0.05$).

Histopathological findings

In the mice that received 80 mg/kg phenol, the kidney showed hyperemia. Th is alteration, as well asmoderate interstitial lymphoplasmacytic nephritis, was observed in the group receiving 180

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mg/kg. At320 mg/kg, severe interstitial lymphoplasmacyticnephritis and necrosis of the renal tubules were also observed (Table 1) Other parts ofthe kidney showed no pathological changes.

Ultrastructural findings

Changes including reduction in the number and size of the microvilli in the epithelial cells of the proximal convoluted tubules (PCTs), deformation and shrinkage of the nuclei, deformity in the shape of the mitochondria and folding of the cytoplasm of the epithelial cells of the PCTs, dilation in the urinary space of the renal corpuscles, and formation of endothelial electron-dense deposits (EEDs) in the basement membranes of the glomeruli were seen in the mice that received phenol.

TABLE:1 histological changes in the kidney of mice exposed to diff erent concentrations of phenol by the gavage method for 10 days .

Findings / groups	80 mg /kg phenol daily	180mg/kg phenol daily	320mg/kg phenol daily
Necrosis of renalt tubule	-	-	++
Interstitial lymphoplasacytic nephritis	++	++++	++++
Hyperemia	+++	++	++++

Lesion described as (++++): a dominant change in all of the animals of each group; (+++): a relatively common change in all of the animals of each group; (++): a change in all of the animals of each group; (+): a change in a few of the animals of each group.

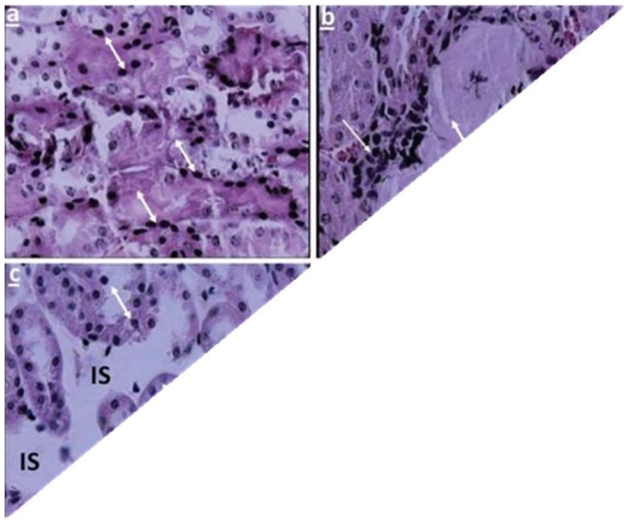

Figure 1 : Kidney transverse sections of the mice treated with phenol at a daily concentration of 320 mg/kg for 10 days continuous days: a) necrosis of the epithelial cells of the renal tubules (double-headed arrows) at 100×, b) massive necrosis of the renal tubules (double-headed arrows) and interstitial lymphoplasmacytic nephritis (arrows) at 400×, c) necrosis of the epithelial cells of the renal tubules (double-headed arrows) and dilation of the interstitial tissue of the kidney (IS) at 100×, d) severe hyperemia in the renal tissue (triangle) at 100×. Hematoxylin and eosin stain.

TABLE: 2 Ultrastructural features of renal lesions observed in mice exposed to diff erent concentrations of phenol by the gavage method for 10 days.

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Renal lesions/groups	80mg/kg phenol daily	180mg/kg phenol daily	320mg/kg phenol daily
Decrease in the number and size of the microvilli in the epithelial cells of thePCTs	+	+++	++++
Deformation and shrinkageof nuclei, malformation of mitochondria and folding of cytoplasm in the epithelial cells of PCTs.	++	++	++++
Dilation of urinary space of the renal corpuscles.	+++	++	+++
Formation of EEDs in the basement membrane of the glomerulus.	+	+	+++

DISCUSSION:

Estimation of the renal excretion of the waste metabolites and histological changes in the kidney has provided useful information on the health status of the kidneys. CRT and BUN are waste products of protein metabolism that have to be excreted by the kidney. Therefore, it is found that increases of CRT and BUN in this study are indicators of the biochemical damage to the kidney. Electrolytes and the water excretion balance are regulated via the kidneys;. Serum concentrations of electrolytes and excretory materials are important measures in assessing the biochemical capabilities of the kidney because they demonstrate the presence or absence of active lesions in the kidney and the biochemical capacity of the different parts of the nephron. Creatinine, urea, and electrolytes (sodium, potassium,

chloride. and bicarbonate) are the most sensitive biochemical markers employed in the diagnosis of renal damage, since CRT and BUN are excreted through the kidney while the electrolytes are reabsorbed and excreted in the tubules.

CONCLUSION:

Phenols are uremic toxins of intestinal origin formed by bacteria during protein metabolism. Of these molecules, p-cresol is the most studied and has been associated with renal function impairment and vascular damage. The effect of phenol, damaged peripheral renal symapathetic nerves .BPA distrupts renal function with phenolic structures, used in the synthesis of polycarbonate plastics and epoxy resins. Exposure of these mainly through the diet, in particular from food & beverages. BPA exposure results from either the release of unpolamerized monomers or the slow decay of polymer bonds, it leads to release of monomer in to liquids and foods. In patients with abnormal kidney function, BPA may accumulate in the serum. The BPA can be

extracted from the device by hydrophobic components present in the blood. In recent studies, chronic use of BPA free dialysers indicate decrease of BPA serum levels in dialysed patients reflecting the effect on inflammation and oxidative stress. The significant increases observed in serum CRT and BUN levels, AIP activity and histopathological changes of the renal tissue in mice exposed to phenonic components indicate tissue injury and it leads to nephrotoxicity.

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