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Research Article

Restorative effect of *Curcuma longa* on arsenic-induced nephrotoxicity in rats

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Abstract

Arsenic is a metalloid that can be toxic to humans and other living organisms, occurs naturally and anthropogenically throughout the world at varying concentrations, including concentrations of concern in soil or groundwater. Presently, in Bihar (India) 16 districts are affected with arsenic poisoning in ground water causing lots of health hazards among the population and presently there is no solution for them. This arsenic intoxication has caused lots of problems related to kidney. The present study investigated the restorative effect *Curcuma longa* (Turmeric) on sodium arsenite induced nephrotoxicity in rats. Sodium arsenite (8 mg/kg/day p.o. 8 weeks) was administered to produce nephrotoxicity in rats followed by administration of *Curcuma longa* (100 mg/kg/day p.o. 4 weeks) to attenuate the arsenic mediated nephro-toxicity. The kidney function tests were assayed and were found with elevated levels of urea, uric acid, and creatinine. Furthermore, their free radical assessment like lipid peroxidation levels were assayed which was found significantly high. But, after administration of aqueous extract of *Curcuma longa,* it caused significant restoration in serum levels of urea, uric acid, creatinine, and lipid peroxidation levels. Thus, it is evident from study that *Curcuma longa* possesses antidote and acts effectively against arsenic induced nephrotoxicity.

Keywords: Arsenic, Nephrotoxicity, Antidote effect, Kidney

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1. Introduction

Arsenic, a metalloid that can be toxic to humans and other living organisms, occur naturally and anthropogenically throughout the world at varying concentrations, including concentrations of concern in soil or groundwater. Acute arsenic exposure harms human health in many ways including the development of malignancies, severe gastrointestinal toxicities, diabetes, cardiac arrhythmias, and death [1]. Natural sources such as volcanic action, erosion of rocks, and forest fires introduce arsenic into the environment [2]. Anthropogenic sources include arsenic added to the soil plant system as insecticides, herbicides, pesticides, livestock dips and wood preservatives. It is estimated that more than 40 million people worldwide are chronically exposed to dangerous levels of arsenic which leads to several diseases, including various types of cancer [3].

Environmental toxins and radiation are suspected to beresponsible in part for the deterioration of semen quality observed worldwide during the recent few decades [4]. Exposure to arsenicals, which is used as herbicides, fungicides and rodenticides may cause soil, air and water pollution and might be a factor considering the hormonal disruption that occurs with its use [5]. Arsenical exposure through drinking water is common in many areas of the world [6]. Metabolic disorders, hypertrophy of adrenal glands [7] and anaemia [8], inhibition of the activity of steroidogenic enzymes [9] and reduction in the weight of the testis and accessory

sex organs [10] are associated with exposure to arsenicals.

Traditional medicines include herbal medicines composed of herbs, herbal materials, herbal preparations, and finished herbal products, that contain as active ingredients parts of plants, or other plant materials, or combinations thereof. Since last two decades, the phytoremediation of various heavy metals borne diseases has gained special attention to researchers.

Present study aims to illustrate restorative effect *Curcuma longa* on arsenic induced nephrotoxicity in rats.

2. Materials and methods

2.1 Animals: Charles Foster rats, weighing 160g to 180g of 8 weeks old, were obtained from animal house of Mahavir Cancer Institute and Research Centre, Patna, India (CPCSEA Regd-No. 1129/bc/07/CPCSEA). The research work was approved by the IAEC (Institutional Animal Ethics Committee) with IAEC No. IAEC/2012/12/04. Food and water to rats were provided *ad libitum* (prepared mixed formulated food by the laboratory itself). The experimental animals were housed in conventional polypropylene cages in small groups (2 each). The rats were randomly assigned to control and treatment groups. The temperature in the experimental animal room was maintained at 22±2$^{\theta}$C with 12 h light/dark cycle.

2.2 Chemicals: Sodium Arsenite (98.5%) manufactured by Biosol Laboratories Pvt. Limited, Kolkata, India was obtained from the Scientific store of Patna.

2.3 Preparation of *Curcuma longa* (Turmeric) aqueous extract: In the present study, dry rhizome of *Curcuma longa* (Turmeric) were purchased from the local market of Patna, Bihar, India The identity of the medicinal plant was confirmed by Dr. Ramakant Pandey (Botanist), Department of Biochemistry, Patna University, Patna, Bihar, India. The collected rhizomes of *Curcuma longa* were shade dried and were grinded to fine powder. The aqueous extract dose was calculated after LD^{50} estimation which was found to be 1600mg kg^{-1} body weight and the final dose was fixed to 100mg kg^{-1} body weight.

2.4 Experimental design: The control group of 6 rats received distilled water as drinking water. The treatment groups (n= 12) received Sodium arsenite daily at the dose of 8 mg kg^{-1} body weight for 8 weeks orally (after estimation of LD_{50} value which was found to be 60 mg kg^{-1} body weight) followed by administration of *Curcuma longa* 100 mg kg^{-1} body weight daily by gavage method for 4 weeks. Rats were sacrificed after completion of their treatment and there blood was collected and serum was extracted for urea, uric acid, creatinine and lipid peroxidation estimation.

2.5. Biochemical evaluation: The Kidney Function Test (KFT) were assayed by methods as Urea by [12,13], Uric acid by [14] and Creatinine by [15].

2.6. Lipid peroxidation (LPO): Thiobarbituric acid reactive substances (TBARS), as a marker for LPO, were determined by the double heating method [16]. The principle of the method was a spectrophotometric measurement of the color produced during the reaction to thiobarbituric acid (TBA) with malondialdehyde (MDA). For this purpose, 2.5 ml of 100 g/l trichloroacetic acid (TCA) solution was added to 0.5 ml serum in a centrifuge tube and incubated for 15 min at 90$^{\theta}$C. After cooling in tap water, the mixture was centrifuged at 3000g for 10min, and 2 ml of the supernatant was added to 1 ml of 6.7 g/l TBA solution in a test tube and again incubated for 15 min at 90$^{\theta}$C. The solution was then cooled in tap water and its absorbance was measured using Thermo Scientific UV-10 (UV–Vis) spectrophotometer (USA) at 532nm.

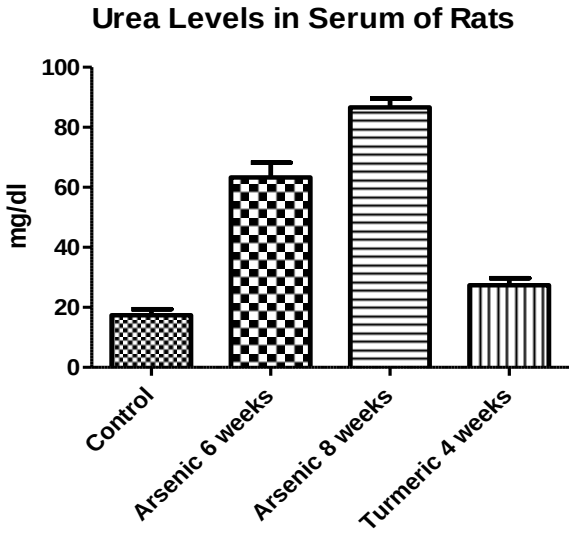
2.7. Statistical analysis: Results are presented as mean ± SD and total variation present in a set of data was analysed through one way analysis of variance (ANOVA). Difference among mean values has been analysed by applying Dunnett's t-test. Calculations were performed with the Graph Pad Prism Program (Graph Pad software, Inc., San Diego, U.S.A.). The criterion for statistical significance was set at $P< 0.05$.

3. Result

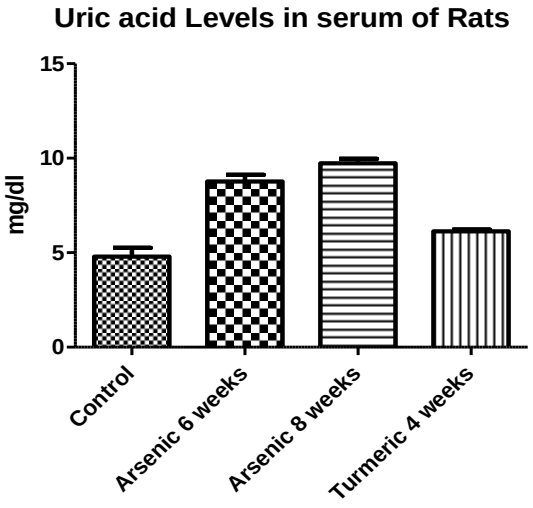
Urea levels in control rat was 17.33 ± 2.02 mg/dl while in sodium arsenite 6 weeks and 8 weeks treated group it was 63.33 ± 4.91 mg/dl and 86.67 ± 2.96 mg/dl. In turmeric administered group of rat urea levels was 35.67 ± 1.20 mg/dl after 8 weeks (Graph Figure 1). Uric acid levels in control rat was 4.800 ± 0.45 mg/dl while in arsenic 6 weeks and 8 weeks treated group it was 8.767 ± 0.34 mg/dl and 9.733 ± 0.23 mg/dl. In turmeric administered group of rat uric acid levels was 6.130 ± 0.09 mg/dl after 8 weeks (Graph Figure

2). Creatinine levels in control rat was 0.5167 ± 0.03 mg % while in arsenic 6 weeks and 8 weeks treated group it was 8.767 ± 0.34 mg % and 9.733 ± 0.23 mg %. In turmeric administered group of rat creatinine levels was 6.130 ± 0.09 mg % after 8 weeks (Graph Figure 3).

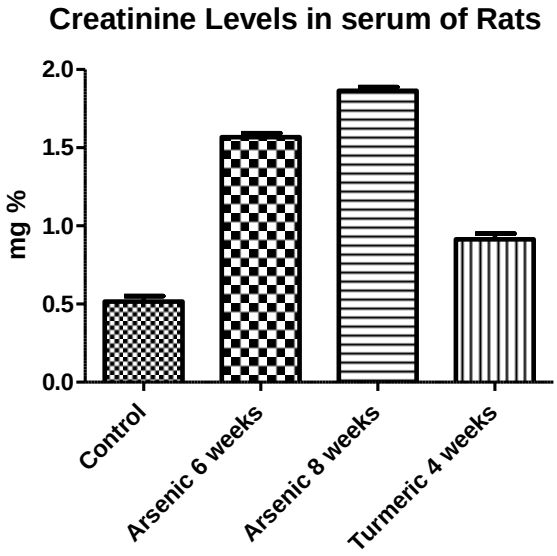
Lipid peroxidation levels in control rat was 1.987 ± 0.06 nmol/ml while in arsenic six weeks and eight weeks treated group it was 41.93 ± 1.19 nmol/ml and 58.73 ± 1.36 nmol/ml. In turmeric administered group of rat lipid peroxidation levels was 8.060 ± 0.21 nmol/ml after 8 weeks (Graph Figure 4).



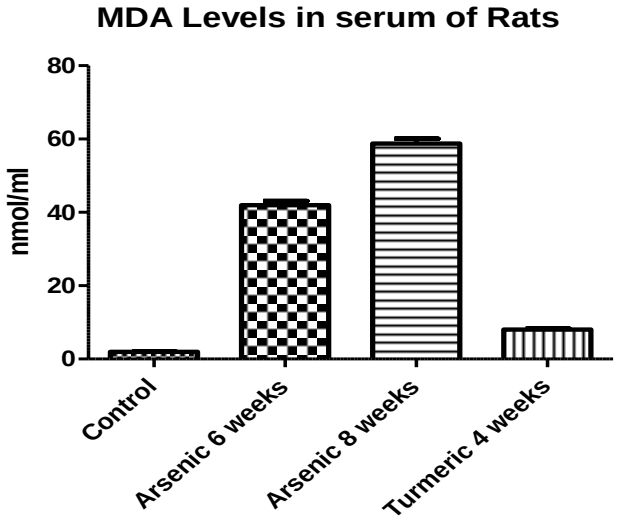
Graph Fig. 1: Effect of Turmeric on Arsenic induced toxicity showing Urea activity (n=6, values are mean± S.D)



Graph Fig. 2: Effect of Turmeric on Arsenic induced toxicity showing Uric acid activity (n=6, values are mean± S.D)



Graph Fig. 3: Effect of Turmeric on Arsenic induced toxicity showing Creatinine activity (n=6, values are mean± S.D)



Graph Fig. 4: Effect of Turmeric on Arsenic induced toxicity showing Lipid peroxidation activity (n=6, values are mean± S.D).

4. Discussion

Exposure to arsenic is associated with various metabolic disorders, hypertrophy of adrenal gland [17] and anemia [18]. A number of proteins and enzyme systems containing sulfhydral group have been found to be altered by arsenic [19]. Arsenic effects mitochondrial enzymes and impairs tissue respiration, which seems to be related to the cellular toxicity [20]. Gonadal effects of arsenic were fist evaluated in rat, then in fishes [21,22]. Most of the available data on arsenic toxicity indicates that the main concern is with the developmental toxicity on the fetus [23].

The kidney and liver are considered to be the most susceptible organs for metals, because these organs contain most of the metallothionein binding toxic metals [24-28]. These toxic metals also produce free radicals such as lipid peroxides [29]. In present study urea, uric acid, creatinine and lipid peroxidation levels increased many folds in arsenic administered group of rats.

Phytoremediation of rhizome extracts of *Curcuma longa* has been well documented on its antibacterial, antiamoebic, and anti-HIV effects and also shows antioxidant [30,31], antitumour [32] and anticarcinogenic activities [33,34]. In present study *Curcuma longa* administration causes marked restoration in urea, uric acid, and creatinine. Lipid peroxidation levels were also restored effectively in turmeric administered group of rats. *Curcuma longa* bears a vital constituent curcumin which is a highly pleiotropic molecule that was first shown to exhibit antibacterial activity in 1949 [35]. Since then, this polyphenol has been shown to possess anti-inflammatory, hypoglycemic, antioxidant, wound-healing, and antimicrobial activities [36]. Curcumin also has some protective role against arsenic-induced DNA damage [37-38]. Thus, *Curcuma longa* possesses restorative activity against arsenic induced nephrotoxicity.

Conclusion

It is evident from study that *Curcuma longa* acts effectively against arsenic induced nephrotoxicity. It restores Kidney function test effectively. It also restores lipid peroxidation levels up to the normal levels, thus indicates that *Curcuma longa* plays promising role and protects kidney from arsenic induced nephrotoxicity efficiently.

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