

Ameliorating Effect of *Cucumis sativus* (Cucumbers) against Arsenic Induced Toxicity in Mice

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Abstract

In the entire world, about 200 million populations are exposed to arsenic poisoning in groundwater. Arsenic is a very poisonous metalloid and has three allotropic forms. The toxic inorganic arsenic is converted and utilized metabolically into organic form. It is primarily eliminated out from the human body through metabolic wastes like urine and is also deposited in the hair, nails and skin of the affected ones. Arsenic is known to be a carcinogen as Carcinogen category 1 in the forms of arsenic trioxide, arsenic pentoxide, arsenous acids, arsenic acid and their salts. The arsenic also affects the epidermal system, the nervous system and the vascular system of humans. In the present investigation for toxicological evaluation of arsenic Liver Function Tests & Kidney Function Tests have been considered. It is presumed that medicinal plants have significance in the present day in view of the lethal diseases like AIDS, cancer, hepatitis, nephritis sterility too for which no effective drugs are found till today in modern system of medicine. Medicinal plant based drugs generally have no side effects or the least side effect. Thus to evaluate an ameliorating effect, if any, to mitigate the arsenic toxicity in mice, for which *Cucumis sativus* (cucumbers) has been taken as curative measure. Sodium arsenite at the dose of 3 mg/kg body weight was administered for 4 weeks followed by the administration of *Cucumis sativus* (cucumbers) for 4 and 6 weeks at dose of 500 mg/kg body weight. Their biochemical levels like liver and kidney function tests were assayed and were found with elevated levels. But, after administration of aqueous extract of *Cucumis sativus* (cucumbers), there was significant amelioration in the biochemical levels. The protective effect of *Cucumis sativus* (cucumbers) was shown in the form of normalization of enzymatic and non-enzymatic activities represented by normalization

of liver and kidney functions.

Keywords

Arsenic, Hepatotoxicity, Renal Toxicity, *Cucumis sativus* (Cucumbers)

1. Introduction

Arsenic is a systemic poison, and chronic ingestion of arsenic can lead to a wide range of health problems, which are collectively called *arsenicosis* or chronic arsenic poisoning. The effects include skin lesions, cancer of the skin, lung a bladder, and gastro-intestinal and pulmonary condition. In the recent times it has caused serious health issues in the population worldwide. Arsenic toxicity through groundwater arsenic contamination is the world's biggest natural groundwater calamities which got a huge impact on global public health. India is facing the consequences of arsenic poisoning mainly in the area of Ganga Brahmaputra fluvial plains. Arsenic is considered to be major environmental health disaster [1] [2] [3]. It is estimated that more than 200 million people are exposed to high level ($<10 \mu\text{g L}^{-1}$) of arsenic toxicity through drinking water [4].

Liver is the organ which not only carries out the metabolic functions but also detoxifies the toxins. In arsenic exposure, arsenate is actively transported into cells by phosphate transporters in liver [5]. Kidneys accumulate arsenic in the presence of repeated exposures. The kidneys are the major route of arsenic excretion, as well as major site of conversion of pentavalent arsenic into the more toxic and less soluble trivalent arsenic. Sites of arsenic damage in the kidney include capillaries, tubules, and glomeruli [6].

In various studies it has been observed that cucurbitacins present in *C. sativus* exhibited cytotoxicity and anti-cancer activity. Besides this, cucurbitacins also exhibited wide ranges of *in-vitro* or even *in-vivo* pharmacological effects and in used as purgative, anti-inflammatory and anti-fertility agent [7].

In the present study, cytoprotective effect of seeds of *Cucumis sativus* (Cucumber) was done on sodium arsenite induced liver and kidney injury through biochemical assay. No such study on the antidote effect of *C. sativus* on arsenic has been carried out till date. Therefore, the present study is designed to evaluate ameliorating effect of *Cucumis sativus* (cucumbers) to mitigate the arsenic toxicity in mice.

2. Materials and Methods

Animals: Swiss albino mice (*Mus musculus*), weighing 30 g to 35 g 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. 2015/3E-16/12/15. Food and water to mice 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 $22^{\circ}\text{C} \pm 2^{\circ}\text{C}$ with 12 h light/dark cycle.

Chemicals: Sodium Arsenite (98.5%) manufactured by Sigma-Aldrich, USA (CAS Number: 7784-46-5), was obtained from the Scientific store of Patna of Bihar India.

Medicinal plant used: Seed extract of *Cucumis sativus* (cucumbers) was used as antidote.

Preparation of *Cucumis sativus* (cucumbers) aqueous extract: In the present study, seed of *Cucumis sativus* (cucumbers) were procured locally from Patna, Bihar, India. The identity of the medicinal plant was confirmed by Dr. Ashok Ghosh (Botanist), Department of Botany, Magadh University, Bihar, India. The collected seed of *Cucumis sativus* (cucumbers) were dried and were grinded to fine powder. The aqueous extract dose was calculated after LD_{50} estimation which was found to be 4000 mg kg^{-1} body weight and the final dose ($1/8^{\text{th}}$ dose) was fixed to 500 mg kg^{-1} body weight as maximum permissible dose (MPD).

Chronic Toxicity Study: Selected pathogen-free mice were sorted and sodium arsenite was administered at the dose of 3 mg/kg body weight dose for 4 weeks by Gavage method. Sacrifices were done at the end of 4^{th} week of Sodium arsenite administration in each group.

Bioremediation: Sodium arsenite administration 3 mg/kg body weight for 4 weeks was followed by the administration of seed of *Cucumis sativus* (cucumbers) for 6 weeks at the dose of 500 mg/kg body weight. Animals were sacrificed on 6^{th} weeks of administration.

Biochemical Assessment: Blood samples were collected by orbital puncture and centrifuged to separate the serum to carry out biochemical analysis. Biochemical analysis were performed through serum by standard kit process (Coral crest) through U.V Vis spectrophotometer. The Liver Function Tests (LFT) tests like Serum Glutamate Pyruvate Transaminase (SGPT), Serum Glutamate Oxalate Transaminase (SGOT), Alkaline Phosphatase (ALP) and Bilirubin tests were carried out while in Kidney Function Tests (KFT) Urea, Uric Acid and Creatinine tests were carried out.

Statistical Analysis: Results are presented as mean \pm S.D and total variation present in a set of data was analysed through one-way analysis of variance (ANOVA). Difference among means has been analysed by applying Dunnett's "t" test at 99.9% ($p < 0.05$) confidence level. Calculations were performed with the GraphPad Prism Program (GraphPad Software, Inc., San Diego, USA).

3. Results

In the present study *Cucumis sativus* (cucumbers) seed extract treatment after

6th weeks showed a significant change in the Biochemical parameter. Following the *Cucumis sativus* (cucumbers) treatments, after 6 weeks the SGPT, SGOT, ALP and Bilirubin concentrations in the arsenic-treated mice decreased from 209.7 ± 6.74 U/ml to 54.00 ± 2.18 U/ml in SGPT level, from 128.7 ± 2.60 U/ml to 36.33 ± 1.32 U/ml in SGOT level, from 29.67 ± 1.76 K.A. Unit to 11.07 ± 0.49 K.A. Unit in ALP level, from 1.677 ± 0.06 mg/dl to 0.9100 ± 0.04 mg/dl in bilirubin levels respectively, compared with the post-arsenic values (Table 1).

Following the *Cucumis sativus* (cucumbers) treatments, after 6 weeks the Urea, Uric acid, and creatinine concentrations in the arsenic-treated mice decreased from 86.67 ± 2.96 mg/dl to 39.07 ± 1.02 mg/dl in Urea level, from 9.733 ± 0.23 mg/dl to 7.230 ± 0.09 mg/dl in Uric acid level, from 3.733 ± 0.23 mg% to 1.95 ± 0.14 mg% in creatinine levels respectively, compared with the post-arsenic values (Table 2).

4. Discussion

In the present study, cytoprotective effect of seeds of *Cucumis sativus* (Cucumber) was observed on sodium arsenite induced liver and kidney injury through biochemical assay and histopathological study is an exclusively new work added in the field of toxicology. The findings show restoration in parameters of liver function tests and kidney function tests, as compared to sodium arsenite induced toxicity. The biochemical assay showed decrease in the levels of SGPT, SGOT, ALP, bilirubin, urea, uric acid and creatinine. This denotes that *Cucumis*

Table 1. Changes in Liver Function Test of mice exposed to Sodium arsenite at the dose of 3 mg/Kg body weight daily for 6 weeks and its amelioration by *Cucumis sativus* (cucumbers) for 6 weeks.

Biochemical Parameters	Control (n = 6)	Arsenic four weeks (n = 6)	<i>Cucumis sativus</i> Six weeks (n = 6)
SGPT (U/ml)	25.67 ± 1.20	209.7 ± 6.74	54.00 ± 2.18
SGOT (U/ml)	22.00 ± 2.64	128.7 ± 2.60	36.33 ± 1.32
ALP (K.A Units)	6.567 ± 0.35	29.67 ± 1.76	11.07 ± 0.49
Bilirubin (mg/dl)	0.5633 ± 0.029	1.677 ± 0.06	0.9100 ± 0.04

The data are presented as mean \pm S.D, n = 6, significance at $p < 0.0001$.

Table 2. Changes in Kidney Function Test of mice exposed to Sodium arsenite at the dose of 3 mg/Kg body weight daily for 6 weeks and its amelioration by *Cucumis sativus* (cucumbers) for 6 weeks.

Biochemical Parameters	Control (n = 6)	Arsenic four weeks (n = 6)	<i>Cucumis sativus</i> Six weeks (n = 6)
Urea (mg/dl)	17.33 ± 2.02	86.67 ± 2.96	39.07 ± 1.02
Uric acid (mg/dl)	4.800 ± 0.45	9.733 ± 0.23	7.230 ± 0.09
Creatinine (mg%)	0.5167 ± 0.03	3.733 ± 0.23	1.95 ± 0.14

The data are presented as mean \pm S.D, n = 6, significance at $p < 0.0001$.

sativus played vital role to combat the side effects of sodium arsenite.

The seeds of cucumber are rich by the number of constituents including crude proteins (42%) and fats (42.5%). The ash is rich with phosphate (P_2O_5 , 0.62%). The extracted oil from seeds is clear and light yellow with specific gravity of 0.91; acid value 0.22; saponification value 1930; soluble fatty acid (as butyric acid) 0.4% and unsaponification matter (0.91%). The fatty acid components are palmitic (0.63%), stearic (16.2%), linoleic (40.11) and oleic acid (38.70) [8]. It contains a number of sterols such as codisterol, 25 (27)-dehydroporifersterol, cle-rosterol, isofucosterol, stigmasterol, campesterol, 22-dihydrobrassicasterol, sitosterol, 25 (27)-dehydrofungisterol, 25 (27)-hydrocondrillasterol, 24- β -ethyl-25 (27)-dehydrofungisterol, avenasterol, 22-dihydrispinosterol and 24-methylenecolesterol [9]. The gibberellin hormone is also found in seeds. Seed cake contains water (1.13%) protein (72.53%) ash (9.7%), crude fiber (1%) and carbohydrates (8.64%).

In various studies it has been observed that Cucumber extract showed anti-oxidant activities against various assays including DPPH reduction assay, total oxyradical scavenging capacity (TOSC) assay, trolox equivalent antioxidant capacity (TEAC), total radical-trapping antioxidant parameter (TRAP) or ferric reducing-antioxidant power (FRAP) assays [10] [11] [12]. Melo *et al.* [13] reported the polyphenol contents in cucumber. Total phenolic contents, flavonols and proanthocyanidins were found to be 9.05 ± 0.83 , 2.06 ± 0.09 and 55.66 ± 1.52 mg/100 g respectively in cucumber extract. The whole extract contains high concentrations of ascorbic acid (1.49 ± 0.85 mg/100 g) also (Melo *et al.* 2006). Like one more study, free phenolics content in cucumber was found to be 14.37 ± 1.48 mg/100 g of sample (73.8%), when it was examined along with another 10 vegetables [14]. In this experiment bound phenolic compounds as Bound-E and Bound-W were found to be 2.92 ± 0.07 (15%) and 2.17 ± 0.06 (11.2%) mg/100 g of sample respectively with high percentages of vitamin C (23.5%).

Other effects of Cucurbitaceae plants of Indian origin including *C. sativus* have been well studied for blood sugar lowering potential at dose of 250 mg/kg by oral administration, it was found that the fruit does not affect the blood sugar level or depress the peak value, after glucose load [15], whereas another study suggested that *C. sativus* decreases significantly the area under the glucose tolerance curve and the hyperglycemic peak on 27 healthy rabbits [16]. The oral administration of the pectin extracted from the fruit of *C. sativus* at a dose of 5 g/kg body weight/day showed significant hypolipidemic action in normal as well as cholesterol-fed experimental animals [17]. Allen [18] studied that lectin from the exudates of the fruit of the cucumber having an anti-parasitic function that strongly inhibited by chitin oligosaccharides.

The seeds are useful for quitting burning sensation, constipation, tonic and intermittent fevers [19]. Gill *et al.* [20] suggested that the methanolic extract of *C. sativus* seeds possessed significant ulcer potential which could be due to the antioxidant activity at a dose of 300 mg/kg in pyloric ligation and water immer-

sion stress induced rat models. The induction effect of UV-B on the antioxidant enzymes such as superoxide dismutase (SOD), guaiacol peroxidase (POD), ascorbic acid peroxidase (APX) and glutathione reductase (GR) and its suppressed modulation to detoxify excess ROS via external application of α -tocopherol and benzoquinone in cucumber cotyledons have also been examined [21]. Boiled leaves with cumin seeds are useful for throat infection. Powdered leaf with sugar acts as a diuretic and it is also given to treat remitted and inflammatory fevers [22].

Therefore, the *Cucumis sativus* possesses ameliorative effect against arsenic induced toxicity in mice protecting the liver from its deleterious effects.

5. Conclusion

Thus, it is evident from entire study that *Cucumis sativus* plays a very effective and vital role in controlling deleterious effect caused by sodium arsenite by normalizing the biochemical parameters of liver and kidney.

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