

The possible protective effect of *Coriandrum sativum* seeds methanolic extract on hepato-renal toxicity induced by sodium arsenite in albino rats

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ARTICLE INFO

Article history:

Received on: 28/09/2014

Revised on: 22/10/2014

Accepted on: 06/11/2014

Available online: 29/12/2014

Key words:

Coriandrum sativum, Sodium arsenite, Hepato-renal functions, RNA and DNA fragmentation, Apoptosis.

ABSTRACT

This work has been carried out in order to investigate the possible ameliorative effect of Coriander seeds methanolic extract (CSE) on sodium arsenite (As) – induced toxicity in albino rats. 2,3 Dimercaptosuccinic acid (DMSA) was used as a standard chelating agent. The experiment lasted for 8 weeks and blood samples were withdrawn 4 and 8 weeks after As and other treatments administrations. As was used to induce hepatotoxicity in rats in a dose equivalent to 100 p.p.m. In-vivo studies using the different biochemical techniques employed in hepato-renal functions as well as liver apoptotic DNA and total RNA alterations proved that As caused a significant increase in parameters concerned to hepato-renal toxicity while treatment of CSE or DMSA caused an ameliorative effect on this toxicity. Administration of CSE and DMSA together along with arsenite proves the synergistic effects of these chelating agents on arsenite toxicity.

INTRODUCTION

In the recent years, human exposure to different pollutants e.g pesticides, herbicides, fungicides, chemical substances, food additives, smoking, synthetic drugs, cars waste and heavy metals which cause many dangerous diseases such as hepato-renal failure, coronary heart disease and different tumors. Liver is the main target for these pollutants. It plays an essential role in the metabolism of all foreign compounds entering the body (Sharma *et al.*, 2012). Arsenic is one of the environmental pollutants which affect nearly all organ systems. Arsenic-induced oxidative damages. Administration of sodium arsenite reduced the activities of antioxidant enzymes, superoxide dismutase, catalase, glutathione S-transferase and glutathione reductase and glutathione peroxidase as well as depleted the level of reduced glutathione and total thiols (Manna *et al.*, 2007). In addition, sodium arsenite also increased the activities of serum

marker enzymes, alanine transaminase and alkaline phosphatase, enhanced DNA fragmentation, protein carbonyl content, lipid peroxidation and the level of oxidized glutathione. In humans, inorganic arsenic is reduced nonenzymatically from pentoxide to trioxide, using glutathione (GSH) or it is mediated by enzymes. Reduction of arsenic pentoxide to arsenic trioxide increases its toxicity and bioavailability. Inorganic-arsenic is methylated to monomethylarsenic acid and finally to dimethylarsinic acid. Thus, arsenic exposure may cause DNA hypomethylation due to continuous methyl depletion, facilitating aberrant gene expression that result in carcinogenesis (Reichard and Puga, 2010). The effects of arsenic on expression of cancer-related genes in rat liver following subchronic exposure to sodium arsenate (100 ppm in drinking water) was investigated by (Xing *et al.*, 2004). Conventional drugs used in the treatment of liver disease are often inadequate, therefore it is necessary to search for alternative drugs. So, scientists call for coming back to nature in order to use of the medicinal plants, herbs and natural products to overcome the problems due to the different pollutants.

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Plants contain many components which have antioxidant properties e.g vit. C, vit. E, carotenes, flavonoids, tannins and other phenolic compounds (Parekh *et al.*, 2012). *Coriandrum sativum*, a glabrous, aromatic, herbaceous annual plant, is well known for its use in the treatment of many diseases. It is a major component of many hepatoprotective herbal formulations. Pandey *et al.*, (2011) was mentioned that *C. sativum* possess diuretic, carminative, digestive, anthelmintic, antioxidant and antibacterial activities. A large number of phytoconstituents, viz essential oils, flavonoids, fatty acids and sterols have been isolated from different parts of *C. sativum*. which reported to have a very effective antioxidant activity profile showing 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, lipoxygenase inhibition, phospholipid peroxidation inhibition, hydroxyl radical scavenging activity, superoxide dismutation and glutathione reduction. The ethanolic, methanolic, chloroform, ethyl acetate and water extracts of *C. sativum* have high total phenolic content with the presence of different constituents such as pyrogallol, caffeic acid and glycitin. The present study was designed to evaluate the possible protective effect of *C. sativum* seeds methanolic extract on the arsenite induced hepato-renal toxicity in albino rats compared with DMSA as a reference chelating agent.

MATERIALS AND METHODS

Materials

Tested Plant

The seeds of *Coriandrum sativum* L. (Apiaceae family) were collected from National Organization for Drug Control and Research (NODCAR) field, Giza, Egypt.

Meso 2, 3-dimercaptosuccinic acid (DMSA) (as thiol chelator reference agent)

DMSA is a known orally effective chelating agent for childhood lead and arsenic poisoning. It has two sulfhydryl groups and has been shown to possess antioxidant properties. It was supplied from Sigma Chemicals Co. (St Louis, MO, USA).

Sodium rsenite (hepatotoxic agent)

Arsenic salts are considered as important environmental toxicants that have both natural and industrial sources. They have been shown to induce oxidative tissue damage.

Chemicals

All chemicals and reagents, either analytical or purified grade, were purchased from Sigma and Aldrich Chemicals Company (St Louis, MO, USA)

Experimental Animals

The study was conducted using 60 female Swiss strain albino rats weighing about 150 ± 10 g and obtained from the animal house of National Organization for Drug Control and Research (NODCAR), Giza, Egypt. Animals were kept under standard laboratory conditions and fed on normal basic diet. They

were acclimatized to the new environment for a week prior to the experiment.

Methods

Preparation of Plant Extract

Seeds of the selected plant were collected, dried and grounded to fine powder and then soaked in 80% methanol for 48 hrs on an orbital shaker at room temperature. Extracts were filtered and the residue was re-extracted under the same conditions until extraction solvents became colorless. The combined filtrates were concentrated till dryness under reduced pressure at 40°C using a rotary evaporator and then the concentrated extract was lyophilized.

Experimental design

To study the protective effect of Coriander seeds methanolic extract (CSE) against hepato-renal toxicity, a total of 60 rats were used and the experiment lasted for 8 weeks. Animals were divided randomly into equal 5 groups (12 rats each) as follows:

- **Group 1:** served as negative control.
- **Group 2: (As),** rats received a daily dose of sod. arsenite in drinking water equivalent to 100 ppm and served as positive control group (Hassan *et al.*, 2003).
- **Group 3: (As + CSE),** rats received daily oral dose of sod. arsenite and daily single oral dose (1 g /kg b.w.) of CSE (Taherian *et al.*, 2012) for 8weeks.
- **Group 4: (As + DMSA),** rats received sod.arsenite and oral dose of DMSA (0.05 g/kg b.w.) orally for 5 days lasted (Flora *et al.*, 2005).
- **Group 5: (As + CSE + DMSA),** rats received sod. Arsenite and CSE for 8weeks then DMSA only for the last 5 days of 8 weeks.

The experiment lasted for 8 weeks and the blood samples were withdrawn at 0 time, 4 and 8 weeks after the start of administrations. At the end of the experiment, all animals were killed by decapitation and their livers were rapidly dissected, washed from blood by ice-cold isotonic saline, blotted between two filter papers and weighed for further investigation.

Biochemical Analysis

Serum ALT and AST were determined according to the method described by Reitman and Frankel (1957) and serum ALP by Kind and King (1954). Blood urea was measured according to the method described by Fawcett and Soctt (1960). Creatinine in blood was measured according to the method described by Schirmeister *et al.* (1964).

Evaluation of antimutagenic activity of the tested plants

DNA fragmentation assay:

The method of DNA fragmentation was conducted according to salting out extraction method described by Aljanabi and Martinez (1997) with some modifecations by Hassab El Nabi (2004).

Determination of total RNA

Isolation of RNA was performed according to the method of EZ-10 Spin Column Total RNA Minipreps Super Kit, Canada.

Statistical Analysis

The biochemical results were expressed as mean \pm S.E and statistically analyzed using ANOVA Statistical Package for the Social Sciences (SPSS) version 17.0 according to Snedecor and Cochran (1967) followed by Tukey Multiple Comparison test. Differences were significant at $P < 0.05$ (Frank and Althoen, 1997).

Apoptotic bands of DNA fragmentation appeared and located at 180 bp and its multiples 360, 540 and 720 bp against DNA marker (Hassab El-Nabi, 2004). The intensity of DNA and RNA bands were measured by Biogene software, France as a maximum optical density values (height) where the height is a maximum intensity at 256 grey levels.

RESULTS

Liver index (LI) %

Liver index was calculated according to the formula of Yang *et al* (2005).

$$\text{Liver index \%} = \frac{\text{Liver weight} \times 100}{\text{Body weight}}$$

The protective effect of CSE and DMSA on the liver index % in albino rats after 8 wks of treatment is shown in Table (1).

Data in Table (1) shows that there is a significant increase ($^{###}P < 0.001$) in the liver index % in As- group versus control group after 8 weeks of treatment, While a significant decrease ($^{***}P < 0.001$) was observed in the liver index % in groups treated with CSE, DMSA or DMSA + CSE versus As- group after 8 weeks.

Liver Function Parameters

Serum alanine transaminase (ALT) activity

The protective effect of CSE and DMSA on the ALT enzyme is shown in Table (2).

Data in Table (2) shows that there is a significant increase ($^{###}P < 0.001$) in ALT activity in As-group versus control group after 4 and 8 weeks. While a significant decrease ($^{***}P < 0.001$) was observed in ALT activity in groups treated with CSE, DMSA or DMSA + CSE versus As group after 4 and 8 weeks.

Serum aspartate transaminase (AST) activity

The protective effect of CSE and DMSA on the AST enzyme activity is shown in Table (3).

Data in Table (3) shows a significant increase ($^{###}P < 0.001$) in AST activity in As- group versus control group after 4 and 8 weeks. While there is an observed significant decrease ($^{***}P < 0.001$) in AST activity in groups treated with CSE, DMSA or DMSA + CSE versus As group after 4 and 8 weeks.

Serum alkaline phosphatase (ALP) activity

The protective effect of CSE and DMSA on the ALP enzyme activity is shown in Table (4).

Data in Table (4) shows that there is a significant increase ($^{###}P < 0.001$) in ALP activity in As- group versus control group after 4 and 8 weeks. There is an observed significant decrease ($^{***}P < 0.001$) in ALP activity in group treated with DMSA + CSE versus As group after 4 and 8 weeks, significant decrease ($^{*}P < 0.05$) in ALP activity in group treated with CSE versus As- group after 4 weeks was also observed.

Kidney Function Parameters

Blood urea

The protective effect of CSE and DMSA on blood urea in albino rats is shown in Table (5).

Data in Table (5) shows that there is a significant increase ($^{###}P < 0.001$) in blood urea in As group versus control group after 4 and 8 weeks. While there is an observed significant decrease ($^{***}P < 0.001$) in blood urea in groups treated with CSE, DMSA or DMSA + CSE versus As- group after 4 and 8 weeks.

Serum Creatinine

The protective effect of CSE and DMSA on serum creatinine in albino rats is shown in Table (6).

Data in Table (6) shows that there is a significant increase ($^{###}P < 0.001$) in S.creatinine in As group versus control group after 4 weeks and a significant increase ($^{##}P < 0.01$) in As- group versus control group after 8 weeks. There is an observed significant decrease ($^{**}P < 0.01$) in S.creatinine in group treated with DMSA + CSE versus As group after 4 and 8 weeks and a significant decrease ($^{*}P < 0.05$) in groups treated with CSE after 4 and 8 weeks and DMSA after 4 weeks versus As-group.

Analysis of total genomic DNA damage

The protective effect of CSE and DMSA on total genomic DNA damage in the liver of albino rats after 8 weeks of treatment is shown in Table (7) and Fig. (1,2). The treated groups show DNA values nearly to be similar to that of -ve control with no release of DNA indicating the absence of DNA damage and apoptotic fragmentation when compared with the +ve control values which show apoptotic fragmentation pattern at 180 bp and its multiples.

Analysis of total RNA

As shown in Table (8) and Fig. (3,4). Liver total RNA isolation also shows the protective effects on treated groups when compared with the untreated and As treated group. The intensity of RNA spots for CSE, DMSA and CSE + DMSA shows intermediate values between -ve and +ve control indicating the minimization of stress effect present in As group.

Table 1: The protective effect of CSE and DMSA on the LI (%) in albino rats.

Groups	Body wt. (gm)	Liver wt. (gm)	Liver index (%)	% Variation
Control	191.3 ± 10.08	5.70 ± 0.30	2.98 ± 0.04	-
As	182.5 ± 6.20	8.87 ± 0.38	4.86 ± 0.20 ^{###}	↑ 63.1 %
As + CSE	196.9 ± 5.42	6.50 ± 0.19	3.30 ± 0.06 ^{***}	↑ 10.7 %
As + DMSA	197.3 ± 8.28	6.40 ± 0.34	3.24 ± 0.05 ^{***}	↑ 8.7 %
As + CSE + DMSA	170.6 ± 5.86	5.54 ± 0.22	3.24 ± 0.08 ^{***}	↑ 8.7 %

Values represent the mean ± S.E.

ns: non – significant, Significant at ^{###}*P* < 0.001 against control. Significant at **P* < 0.05; ***P* < 0.01; ****P* < 0.001 against As.

Table 2: The protective effect of CSE and DMSA on the ALT activity in albino rats (U/L).

Groups	Time intervals (weeks)				
	0	4	% variation	8	% variation
Control	24.0 ± 1.09	22.8 ± 1.12	5.0↓	24.7 ± 0.42	2.9↑
As	22.4 ± 0.60 ^{ns}	44.8 ± 1.09 ^{###}	100↑	51.8 ± 1.06 ^{###}	131↑
As + CSE	23.2 ± 1.09 ^{ns}	26.6 ± 0.94 ^{***}	14.6↑	26.8 ± 1.87 ^{***}	15.5↑
As + DMSA	22.6 ± 0.82 ^{ns}	30.8 ± 2.04 ^{***}	36.3↑	26.9 ± 0.76 ^{***}	19.0↑
As + CSE + DMSA	22.2 ± 0.82 ^{ns}	23.6 ± 0.84 ^{***}	6.3↑	25.5 ± 0.53 ^{***}	14.9↑

Values represent the mean ± S.E.

ns: non – significant, Significant at ^{###}*P* < 0.001 against control. Significant at **P* < 0.05; ***P* < 0.01; ****P* < 0.001 against As.

Table 3: The protective effect of CSE and DMSA on the AST activity in albino rats (U/L).

Groups	Time intervals (weeks)				
	0	4	% variation	8	% variation
Control	60.7 ± 3.18	61.7 ± 2.23	1.6↑	62.3 ± 2.77	2.6↑
As	64.8 ± 1.76 ^{ns}	97.0 ± 3.53 ^{###}	49.7↑	108.4 ± 4.38 ^{###}	67.3↑
As + CSE	59.1 ± 1.72 ^{ns}	70.5 ± 2.28 ^{***}	19.3↑	74.7 ± 2.45 ^{***}	26.4↑
As + DMSA	63.4 ± 2.44 ^{ns}	66.6 ± 1.74 ^{***}	5.0↑	78.8 ± 2.21 ^{***}	24.3↑
As + CSE + DMSA	61.4 ± 0.67 ^{ns}	63.4 ± 2.01 ^{***}	3.3↑	68.2 ± 3.07 ^{***}	11.1↑

Values represent the mean ± S.E.

ns: non – significant, Significant at ^{###}*P* < 0.001 against control. Significant at **P* < 0.05; ***P* < 0.01; ****P* < 0.001 against As.

Table 4: The protective effect of CSE and DMSA on the ALP activity in albino rats (IU/L).

Groups	Time intervals (weeks)				
	0	4	% variation	8	% variation
Control	361.4 ± 7.33	360.7 ± 4.96	0.19↓	378.3 ± 23.39	4.7↑
As	369.7 ± 4.75 ^{ns}	593.7 ± 12.05 ^{###}	60.6↑	539.6 ± 21.61 ^{###}	45.9↑
As + CSE	345.5 ± 19.93 ^{ns}	490.4 ± 26.72 [*]	41.9↑	488.8 ± 32.6 ^{ns}	41.5↑
As + DMSA	386.9 ± 21.20 ^{ns}	523.0 ± 20.55 ^{ns}	35.2↑	495.4 ± 9.95 ^{ns}	28.0↑
As + CSE + DMSA	355.6 ± 9.77 ^{ns}	381.2 ± 30.02 ^{***}	7.2↑	420.6 ± 20.51 ^{***}	18.3↑

Values represent the mean ± S.E.

ns: non – significant, Significant at ^{###}*P* < 0.001 against control. Significant at **P* < 0.05; ***P* < 0.01; ****P* < 0.001 against As.

Table 5: The protective effect of CSE and DMSA on blood urea in albino rats (mg/dl).

Groups	Time intervals (weeks)				
	0	4	% variation	8	% variation
Control	23.3 ± 1.21	24.7 ± 0.98	6.0↑	24.1 ± 0.89	3.4↑
As	25.4 ± 1.86 ^{ns}	58.4 ± 2.21 ^{###}	130↑	60.9 ± 1.51 ^{###}	140↑
As + CSE	26.5 ± 1.30 ^{ns}	38.2 ± 1.53 ^{***}	44.1↑	43.8 ± 0.71 ^{***}	65.3↑
As + DMSA	23.5 ± 0.92 ^{ns}	40.7 ± 1.39 ^{***}	73.2↑	33.2 ± 1.58 ^{***}	41.3↑
As + CSE + DMSA	25.9 ± 1.06 ^{ns}	36.7 ± 1.06 ^{***}	41.7↑	37.7 ± 0.79 ^{***}	45.6↑

Values represent the mean ± S.E.

ns: non – significant, Significant at ^{###}*P* < 0.001 against control. Significant at **P* < 0.05; ***P* < 0.01; ****P* < 0.001 against As.

Table 6: The protective effect of CSE and DMSA on creatinine in albino rats (mg/dl).

Groups	Time intervals (weeks)				
	0	4	% variation	8	% variation
Control	0.38 ± 0.007	0.37 ± 0.016	2.63↓	0.36 ± 0.016	5.26↓
As	0.39 ± 0.009 ^{ns}	0.49 ± 0.006 ^{###}	25.6↑	0.43 ± 0.015 ^{###}	10.3↑
As + CSE	0.36 ± 0.007 ^{ns}	0.42 ± 0.015 [*]	16.7↑	0.37 ± 0.013 [*]	2.77↑
As + DMSA	0.37 ± 0.007 ^{ns}	0.42 ± 0.022 [*]	13.5↑	0.38 ± 0.010 ^{ns}	2.70↑
As + CSE + DMSA	0.38 ± 0.009 ^{ns}	0.41 ± 0.009 ^{**}	7.89↑	0.36 ± 0.008 ^{**}	5.26↑

Values represent the mean ± S.E.

ns: non – significant, Significant at ^{###}*P* < 0.001 against control. Significant at **P* < 0.05; ***P* < 0.01; ****P* < 0.001 against As.

Table 7: The protective effect of CSE and DMSA on total genomic DNA damage in albino rats.

	control	As+ CSE	As+DMSA	As+ CSE +DMSA	As (+ve)
Intact DNA	6095	6385	7145	7133	6843
720bp	-	-	-	-	2174
540bp	-	-	-	-	1640
360bp	-	-	-	-	1888
180bp	-	-	-	-	541

Table 8: The protective effect of CSE and DMSA on total RNA contents in the liver of albino rats.

	control	As+ CSE	As+DMSA	As+ CSE +DMSA	As (+ve)
Total RNA	2730	3945	3880	4435	5935

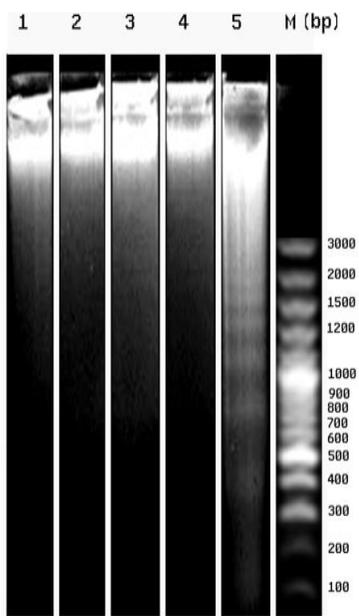


Fig. 1: Digital photograph of total genomic DNA electrophoresis for examples of liver tissues shows the protective effect of CSE against As; L1: control; L2: CSE; L3: DMSA; L4: CSE + DMSA; L5: As and M: DNA marker.

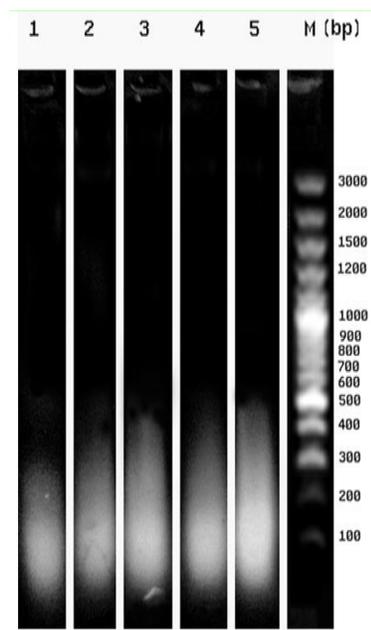


Fig. 3: Digital photograph of total RNA electrophoresis for examples of liver tissues shows the protective effect of CSE against As; L1: control; L2: CSE; L3: DMSA; L4: CSE + DMSA; L5: As and M: DNA marker.

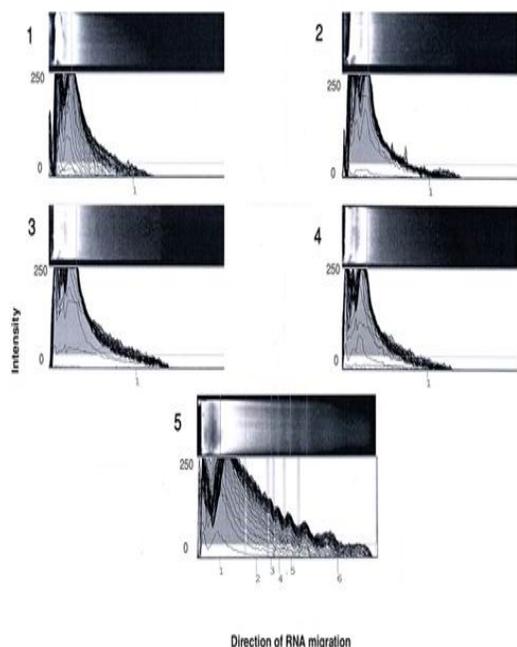


Fig. 2: The analytical peaks for total genomic DNA lanes which resemble the same lanes in Fig. (1) using Biogene software.

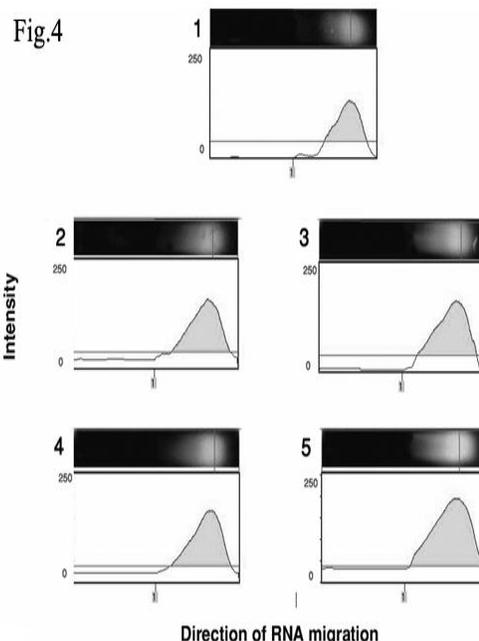


Fig. 4: The analytical peaks for total RNA lanes which resemble the same lanes in Fig. (3) using Biogene software.

DISCUSSION

In this experiment, hepatotoxicity was induced by adding sodium arsenite (100 ppm) in drinking water daily for 8 weeks according to Hassan *et al.*, (2003). Data shows that the significant increase of ALT activities after 8 weeks of treatment. Also, the activity of AST and ALP were significantly elevated due to the administration of arsenite. Our results proved that arsenite caused markable elevations in all biochemical parameters under investigation. These results are agreed with the results of Usuh *et al.*, (2005) and Reichard and Puga, (2010).

In the gut, soluble arsenic compounds present in food or water are rapidly absorbed into the blood stream affecting all body organs. The long-term exposure to arsenic in drinking water can cause thickening, pigment spots and cancer in the skin, lung, bladder and kidney (Yamanka *et al.*, 1990). Administration of arsenite to rats caused also a significant increase in blood urea and serum creatinine (Tables 5,6). Exposure to arsenic compounds is always associated with several human diseases e.g diabetes mellitus, hypertension, tumors, hepato-renal dysfunction (Chen *et al.*, 1992).

Rea *et al.*, (2003) demonstrated that arsenic causes many hazards in human body such as oxidative stress, DNA hypo- or hyper-methylation or alteration of several gene expressions. Microarray analysis provided global changes in expression of gene occurring with arsenic exposure; the aberrantly expressed genes included those involved in cell cycle regulation, DNA damage response, apoptosis and various oncogenes. Yamanaka *et al.*, (2001) mentioned that arsenic causes damage in biological system because of its ability to generate oxidative stress in the cells. Arsenic generates ROS and free radicals like hydrogen peroxide, hydroxyl radical, nitric oxide, superoxide anion, dimethylarsenic peroxy radical and dimethylarsenic radical in living systems. ROS produced leads to the generation of oxidative stress and DNA damage.

Arsenite activates NADH oxidase to produce superoxide ion, which subsequently causes oxidative DNA damage. Hydrogen peroxide and metal ions (Fe^{++} , Cu^{++}) react to produce hydroxyl radicals which react with DNA bases to form adducts which subsequently lead to the formation of strand breaks. Further, arsenic not only causes oxidative DNA damage by production of ROS and other free radicals but it also interferes with repair process of damaged DNA specifically nucleotide excision repair and base excision repair.

In their studies, Liu and Waalkes, (2008) reported that exposure to inorganic arsenic during gestation induces tumors including hepatocellular adenoma and carcinoma, in offspring when they reach adulthood.

The methylated arsenicals, dimethylarsenic acid promotes diethylnitrosamine-initiated liver tumors, whereas trimethylarsine oxide induces liver adenomas and malignant transformation. There is a variety of potential mechanisms for arsenical-induced hepato-carcinogenesis such as oxidative DNA damage, impaired DNA damage repair, acquired apoptotic

tolerance, hyperproliferation, altered DNA methylation and aberrant estrogen signaling. Overall, accumulating evidence clearly indicates that liver could be important target of arsenic carcinogenesis.

The excessive generation of ROS is very damaging: they can attack lipids, proteins and DNA result in lipid peroxidation and DNA mutation leading to several diseases (Singh *et al.*, 2009). Nafisi *et al.*, (2005) mentioned also that arsenic salts can interact with the nucleotides of both DNA and RNA which agree with the obtained results in this study.

Our data illustrated the prophylactic effect of CSE in albino rats against the As salt- induced toxicity. Animals received CSE in a dose equivalent to 1g / kg b.w along with sod. arsenite in drinking water (100 ppm) daily for 8 weeks to show the probable efficacy of this extract on the protection of liver against arsenite toxicity. These data revealed that CSE as well as the chelating agent "DMSA" has an ameliorative effect in all parameters under investigation.

Administration of DMSA + CSE to rats has a synergistic effect in lowering the different parameters used. Our data are in a good agreement with those of Hashim *et al.*, (2005).

Herbal medicines are widely used all over the world. They are often perceived as being natural and therefore harmless. Many herbal remedies individually or in combination with different formulations such as leaves, powder, pastes, decoction, infusion etc. had been recommended to treat various diseases. Many, if not most of medicinal plants contain flavonoids, such compounds have been associated with several beneficial effects such as possessing an antioxidant effect which is considered to be a fundamental property important for life. Many herbs are good source of natural antioxidants and usually their consumption either fresh or dried in the diet should be considered. Therefore herbs are contributed to the daily intake of antioxidant sources.

A large number of plants have been screened as a viable source of natural antioxidants including tocopherols, vitamin C, carotenoids and phenolic compounds which are responsible for maintenance of health and protection from different diseases. Chemical studies on Coriander have shown the presence of some constituents such as quercetin 3- glucuronide linalool, camphor, geranyl acetate, geraniol and cumarins. These active constituents cause the antioxidant properties (Khrenova *et al.*, 1986).

The antioxidative property of Coriander seeds extract may be related to the large amounts of carotenoids, tocopherols and phospholipids (Ramadan and Mörsel, 2004). which act through different mechanisms. Carotenoids act as primary antioxidants by trapping free radicals and as secondary antioxidants by quenching singlet oxygen. Tocopherols and sterols interact with oil surfaces and release hydrogen, inhibiting the propagation step of radical reactions. Synergetic effects were evidenced with combinations of carotenoid and tocopherols. Although the exact mechanism of antioxidative action of phospholipids is not still fully established, these substances would synergistically act with tocopherols, would form barrier for oxygen between air/oil interfaces, would favor formation of mallard like compounds with

oxidation products or would chelate pro-oxidant metals with phosphate groups (Haila *et al.*, 1996). Greenrod and Fenech (2003) reported that phenolic components are considered as protective agents against DNA damage and cytotoxic effects. Several metal chelators have been used to manage the toxicity of heavy metals. DMSA possess a strong antioxidant activity. It is a known orally effective chelating agent for childhood heavy metals poisoning.

It has two sulfhydryl groups and has been shown to possess antioxidant properties (Flora and Tripathi, 1998). In their studies on laboratory animals, Pepcke *et al.*, (1993) revealed the potency of DMSA in reducing lethality and chronic arsenic toxicity. It appears plausible that DMSA could be responsible for the decrease in all indicative parameters of oxidative stress either by removing the toxic metal from the target organs and/or by directly scavenging ROS via its sulfhydryl groups.

CONCLUSION

The present data revealed that sod. arsenite is a potent toxic agent. Coriander seeds methanolic extract (CSE) possess remarkable anti-oxidative behaviour. Administrations of DMSA (chelating agent) along with CSE exhibit a synergistic effect against hepato-renal toxicity. In general we highly recommend the use of medicinal plants and natural products in our diet due to their contents of different components which possess antioxidant activity. CSE is a save prophylactic agent which overcome the possible toxicity caused by certain xenobiotic agents.

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How to cite this article:

Mostafa Saeed, Ahmed Amen, Abdelgawad Fahmi, Islam El Garawani, Sadya Sayed. The possible protective effect of *Coriandrum sativum* seeds methanolic extract on hepato-renal toxicity induced by sodium arsenite in albino rats. *J App Pharm Sci*, 2014; 4 (12): 044-051.