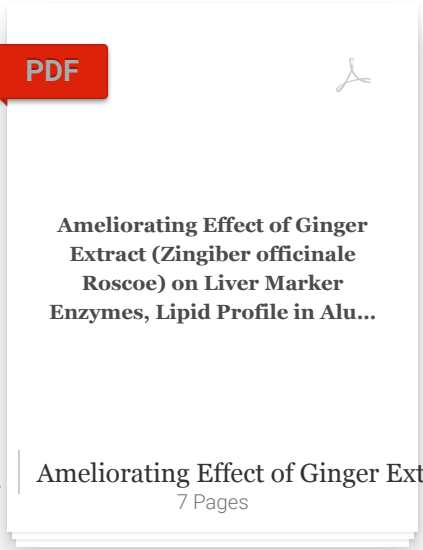

Ameliorating Effect of Ginger Extract (Zingiber officinale Roscoe) on Liver Marker Enzymes, Lipid Profile in Aluminium chloride Induced Male Rats

Available online at www.ijpsdr.com

International Journal of Pharmaceutical Sciences and Drug Research
2015; 7(1): 52-58

Research Article

ISSN: 0975-248X
CODEN (USA): IJPSPP

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ABSTRACT

Nowadays, aluminium (Al) exposure has been increasing and it has the potential to be toxic in animal and humans. In recent years, ginger has become a subject of interest because of its beneficial effects on human health. The purpose of the present study to investigate the effect of ginger extract on serum biochemical parameters of aluminium chloride ($AlCl_3$) induced male rats. 24 Wistar rats (6 in each group) distributed into 4 groups. Control group received distilled water as vehicle; In E1 group, animal received $AlCl_3$ orally (100 mg/kg bw), E2 group received $AlCl_3$ (100 mg/kg bw) and simultaneously with ginger extract (50 mg/kg bw) and E3 group received ginger extract alone (50 mg/kg bw) for 60 days. At the end of the experimental period, blood samples were collected for separating the serum for biochemical analyses. The results showed that oral administration of aluminium revealed a significant increase in the levels of serum glucose, total protein, globulin, albumin, urea, uric acid, creatinine, lipid profile and serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) and no change was noted in bilirubin. The extract of ginger decreased the activities serum levels of AST, ALT, ALP, lipid profile and all the parameter studied. It was concluded that the consumption of ginger protects the liver and kidney against the Aluminium toxicity. In addition, ginger is capable of improving hyperlipidemia and the impaired kidney functions.

Keywords: AST, ALT, ALP, ginger, lipid profiles.

INTRODUCTION

Metallic compounds on land and water pose potential health hazards to living things. Aluminum is the third most prevalent and the most abundant metal in the earth's crust, representing approximately 8% of total mineral components. [1] It is found in our food product, medicines and also added to drinking water for purification purposes. [2] It is widely used in cosmetics, cookware utensils and containers, food additives, structural material in the construction, automotive, aircraft industries, in the production of metal alloys, in the electric industry and in medicine as antacids, antiperspirants. The other uses of aluminium include decorations, fencing, highway signs, cans, dental crowns and dentures. [3] Human exposure to large quantity of aluminium in nature and its many uses is made through intake of major sources i.e. drinking water, food residues, cooking utensils of packaging, food and beverage and aluminum-containing medications. [4]

It is well established that aluminium as neurotoxicant and the different forms of Al have been shown to be systemic toxicants [5]; nowadays, increased attention is

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Received: 18 November, 2014; **Accepted:** 30 December, 2014

being paid to aluminum on various organ systems. Salts of aluminium may bind to DNA, RNA which inhibits enzyme such as hexokinase, acid and alkaline phosphatases, phosphodiesterase and phosphooxydase. [2] Chronic exposition to this element can cause alterations in skeletal, nervous, hematopoietic and respiratory systems. [6-7] Aluminium exposure caused impairments in glucose utilisation, agonist-stimulated inositol phosphate accumulation, free radical-mediated cytotoxicity, lipid peroxidation, reduced cholinergic function, impact on gene expression and altered protein phosphorylation. [8]

The chronic consumption of aluminium produces neuro-toxic effect on humans and animals [9] and has been implicated in several chronic disorders. Liver is considered as the major site for detoxification of toxic metabolites and functions as metabolic centre for various nutrients such as carbohydrates, proteins and lipids [10]; kidney is involved in the elimination of toxic substances. [11] Due to their ability to reabsorb and accumulate metals, kidneys are one of the first target organs of metal toxicity. [12]

Medicinal plants play a key role in human health care. About 80% of the world population relies on the use of

Adult albino rats (Wistar strain) weighing 250-260 g were used in this study. Animals were maintained as per the guidelines of the Institute Animal Ethical Committee. All the animals were housed in polypropylene cages at standard husbandry conditions (Temperature: 23 ± 2°C, Relative humidity: 60-70%, 12h: 12h light /dark cycle) and were provided with standard pellets and water *ad libitum*. They were initially acclimatized for the study. The experimental protocols were approved by the Institutional Animal Ethical Committee (IAEC Approval No 140/PHARMA/SCRI, 2013). After 15 days adaptation period the rats were divided into four groups of 6 animals each.

Experimental groups

Group I – Control group: Rats given water orally, daily for 60 days.

Group II – Experimental group I (E1): Rats given $AlCl_3$ (100 mg/kg body weight) orally, daily for 60 days.

Group III – Experimental group II (E2): Rats given $AlCl_3$ 100 mg/kg body weight simultaneously with ginger extract (50 mg/kg body weight) orally, daily for 60 days.

remedies has been documented. Phytochemical studies showed that ginger is rich in a large number of bioactive substances, including gingerols and shogaols [14] and some related phenolic ketone derivatives. Ginger is used medicinally for its hepatoprotective and antioxidant [15], antidiabetic and hypolipidemic [16-17] and anti-obesity [18] effects. The study by Ajith *et al.*, [19] was carried out to evaluate the protective effect of ginger against cisplatin-induced oxidative stress and acute renal failure in kidneys of mice.

Therefore, our purpose for carrying out this study was to investigate on the effects of ginger on Aluminium toxicity of liver marker enzymes, lipid profile and kidney biomarker.

MATERIALS AND METHODS

Chemicals

Aluminium chloride ($AlCl_3$) was obtained from Sigma Chemical Co. (St Louis, Mo, USA). The dose of $AlCl_3$ (100 mg/kg body weight) was selected based on the study by Priya Anand and Bimla Nehru. [20]

Ginger extracts preparation

The ginger rhizomes were thoroughly washed, peeled, pulverized, and completely dried, coarsely, minced and made into fine powder. The ginger powder was suspended in distilled water and each animal received 0.5 ml of ginger suspension at a dose of 50 mg/kg body weight every day. The low dose of ginger used here is with reference to the average daily intake by human beings, learnt from a survey conducted in India. [21]

Animals

day was recorded and the body weight was taken on every day and the percent changes were calculated. 24 hours after the last treatment, blood samples were collected from the retro-orbital sinus of all animals at the end of the experimental period. The collected blood sample was allowed to clot at room temperature for 20 minutes and centrifuged at 3000rpm for 15 minutes to separate the serum. Serum was used to estimate the biochemical parameters; Glucose, total protein, albumin, bilirubin, ALT, AST, ALP, urea, uric acid, creatinine, cholesterol, triglycerides and high density lipoprotein (HDL) were measured by a RA- 50 Semi Auto analyzer (Bayer) using Siemens Diagnostic kits.

Statistical Analysis

All the data were analyzed using *student t' test* and the data were expressed as mean±SEM. The *P* value of <0.05 was considered to be statistically significant against control.

RESULTS

Effects of oral administration of Aluminium chloride and supplementation of ginger extract on rats serum biochemical parameter is illustrated in Table 1, 2, 3 and 4. Administration of aluminium (E1 group) showed significant increase in glucose (P<0.05), total protein (P<0.001), albumin (P<0.001), globulin (P<0.01) and no change was observed in bilirubin when compared to control animals. While, the administration of ginger extract with aluminium (E2) and Ginger alone (E3) groups maintained the normal levels of value similar to control in above said parameters except protein and albumin. Ginger administration significantly decreased the protein (P<0.05) and albumin (P<0.001) level when compared to control (Table 1).

Table 2 represents the activities of serum AST, ALT and ALP in $AlCl_3$ and ginger treated animals. Aluminium administration significantly increased the activities of ALT (P<0.05), AST (P<0.05) and ALP (P<0.05) when compared to control. There was a normal activity of all enzymes were observed in E2 and E3 groups.

Table 3 illustrates the administration of aluminium significantly increased the level of urea (P<0.01), uric acid (P<0.001), creatinine (P<0.05) and the normal level was observed in ginger administered groups. Further, Table 4 shows the levels of cholesterol, triglycerides and HDL in aluminium chloride and ginger treated animals. As results indicates that aluminium administration showed the significant increase in cholesterol, triglycerides and HDL (P<0.05) when compared to control. But the animals treated with ginger with aluminium chloride and ginger alone groups showed normal levels of lipid profile when compared to control.

Table 1: Protective effect of ginger extract on Al induced liver biomarker

Parameter	Control	$AlCl_3$	$AlCl_3$ + Ginger	Ginger alone
Sugar (mg/dl)	86.6 ± 6.397	108.8 ± 6.795*	97.3 ± 9.048	115.5 ± 8.754
T.Protein(g/dl)	6.0 ± 0.167	8.2 ± 0.438***	6.0 ± 0.423	5.5 ± 0.092*
Albumin(g/dl)	2.8 ± 0.054	3.2 ± 0.062***	2.6 ± 0.163	2.4 ± 0.090**
Globulin(g/dl)	3.2 ± 0.188	5.0 ± 0.418**	3.4 ± 0.188	3.1 ± 0.111
Bilirubin (mg/dl)	0.5 ± 0.021	0.5 ± 0.022	0.58 ± 0.047	0.58 ± 0.030

The results are expressed as Mean ± SEM (n = 6) per treatment and respective control groups. Levels of significance values are *p<0.05, **p<0.01, ***p<0.001 compared with control group. P <0.05 considered to be statistically significant.

Table 2: Ameliorative effect of ginger extract on $AlCl_3$ induced liver marker enzymes

Parameter	Control	$AlCl_3$	$AlCl_3$ + Ginger	Ginger alone
Serum ALP U/L	254.3 ± 11.51	306.3 ± 14.95*	263.0 ± 14.05	260.0 ± 19.13
SGOT (AST) U/L	130.6± 2.367	146.1 ± 5.677*	145.1 ± 8.162	136.6 ± 6.067
SGPT (ALT) U/L	50.0 ± 2.007	60.3 ± 3.223*	57.8 ± 3.309	51.6 ± 3.824

The results are expressed as Mean ± SEM (n = 6) per treatment and respective control groups. Levels of significance values are *p<0.05, **p<0.01, ***p<0.001 compared with control group. P <0.05 considered to be statistically significant.

Table 3: Effect of ginger extract on kidney biomarker of $AlCl_3$ induced rats

Parameter	Control	$AlCl_3$	$AlCl_3$ + Ginger	Ginger alone
Urea (mg/dl)	36.0 ± 1.826	49.1 ± 3.313**	42.6 ± 2.163*	39.3 ± 2.274
Uric acid (mg/dl)	1.03± 0.117	1.91 ± 0.111***	1.45 ± 0.364	1.36 ± 0.123
Creatinine(mg/dl)	0.8 ± 0.030	0.7 ± 0.025*	0.68 ± 0.047	0.76 ± 0.049

The results are expressed as Mean ± SEM (n = 6) per treatment and respective control groups. Levels of significance values are *p<0.05, **p<0.01, ***p<0.001 compared with control group. P <0.05 considered to be statistically significant.

Table 4: Protective effect of ginger extract on lipid profiles of $AlCl_3$ induced rats

Parameter	Control	$AlCl_3$	$AlCl_3$ + Ginger	Ginger alone
Cholesterol(mg/dl)	46.0 ± 4.195	62.8 ± 5.062*	51.6 ± 4.487	49.0 ± 4.159
Triglycerides(mg/dl)	102.6 ± 7.577	129.3 ± 8.268*	117.6 ± 11.44	106. 3 ± 8.289

DISCUSSION

Aluminium is one of the trace elements with toxic effect on living organism. However, in recent years, increased attention is being focused on possible adverse effects of aluminium on human health. The primary effects of aluminium on the liver and kidney function are thought to be mediated via damage to cell membranes.

Glucose, protein, globulin, albumin, Bilirubin

The present study reveals that the administration of aluminium chloride significantly enhanced the levels of serum glucose, total protein, albumin, globulin and no change was observed in bilirubin. Significantly elevated plasma glucose levels were observed in alloxan-diabetic rats fed on aluminium chloride when compared with normoglycemic group. [22-23] The rise in blood glucose may indicate, Aluminium toxicity caused a disruption in carbohydrate metabolism, through enhancement of the breakdown of liver glycogen, possibly mediated by an increase in adrenocorticotrophic and glucagon hormones and/or reduced insulin activity. [24] Significantly enhanced level of glycogen in liver was observed in aluminium chloride treated animals. [25]

In this study, administration of ginger extract significantly reduced serum glucose level when compared with aluminium treated group and the reduction was reached to control animals. Pretreatment with ginger inhibited the induced hyperglycemia and hypoinsulinaemia was reported. [26] Ginger juice significantly lowered the blood glucose in diabetic and non-diabetic animals. [27] Furthermore, the blood glucose was lowered after administration of ethanolic extract of ginger in diabetic rats. [28]

However, the increased level of protein was observed in aluminium treated rats of our findings. It might be due to alterations in protein synthesis or metabolism in