Research Article

Study of Wattakaka Volubilis on Tissue Lipids and Antioxidants in Aluminium Sulphate Exposed Rats

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ABSTRACT

The methanol extract of *Wattakaka volubilis* (L. f) Stapf. (Family: Asclepiadaceae) leaf was investigated for its hepatoprotective effect in male Albino Wistar rats. Hepatotoxicity was induced in Albino rats by administration of aluminium sulphate (50mg/kg, i.p). The ethanol extract of *Wattakaka volubilis* at a dose of 200mg/kg of body weight was administered at single dose per day to for a period of 30 days. The effect of methanol extract of *Wattakaka volubilis* leaf extract on low density lipoprotein (LDL), very low density lipoprotein (VLDL), and high density lipoprotein (HDL), lipoprotein peroxidation (LPO) antioxidant enzymes (catalase (CAT), superoxide dismutase (SOD), reduced glutathione (GSH), glutathione peroxidase (GPx) and glutathione reductase (GR) were measured in the liver toxicity rats. The methanol leaf extract of *Wattakaka volubilis* elicited significant reductions of lipid parameters except HDL, serum enzymes and significantly increased HDL and antioxidant enzymes. From the above results it is concluded that methanol extract of *Wattakaka volubilis* possesses significant, lipids and antioxidant effects in aluminium sulphate exposed rats.

Keywords: *Wattakaka volubilis* extract, Aluminium sulphate, lipid profile, antioxidant enzymes.

INTRODUCTION

The liver is the most complex organ in the body. It plays a vital role in regulatory metabolism processes, performing many essential functions in order to maintain life, such as glycogen storage, production of necessary biochemical for digestion, plasma protein synthesis and detoxification[1,2]. These functions are carried out generally by hepatocytes especially for the process of blood filtration, for chemical digestion of medications, but also against environmental pollution toxins, and alcohol intoxication which can have largely damaging effects over long periods of exposure or abuse[3].

Chronic exposure to aluminium (Al) is a real eventuality due to its high diffusion in manufactured food, water, dust, air and medicines[4]. Despite Al abundance, the amount taken up into cells or organs is very difficult to measure accurately[5]. Only a very small fraction of Al becomes available for absorption (0.1-1%) by the gastrointestinal tract[6] and then most is eliminated by the kidney and to a lesser extent in the bile[7]. Al could be an etiologic factor for different pathologies, such as dialysis syndrome[8], amyotrophic lateral sclerosis[9], Alzheimer's[10,11] and Parkinson's disease[12]. In regard to the liver, this organ possibly plays a role in the metabolism and deposition of Al. Both *in vivo* and *in vitro* studies described Al-hepatotoxicity as a consequence of long exposures[13,14].

The toxic effects of aluminium appear to be mediated, at least in part, by free-radical generation.[15,16] The treatment commonly used in aluminium disorders is desferrioxamine.[17] However, desferrioxamine therapy is associated with undesirable side effects, it is very expensive, and it is only efficient when applied intravenously or subcutaneously.[18]

A stressful condition leads to the excessive production of free radicals which results in oxidative stress an imbalance in the oxidant per antioxidant system. Generation of free radicals is an integral feature of normal cellular functions in contrast to excessive generation and/or inadequate removal of free radical results in destructive and irreversible damage to the cell[19] under normal conditions, there is a natural defence system provided by enzymes such as superoxide Dismutase[SOD], Catalase[CAT] And Glutathione peroxide[GSH-Px) which performs a vital role for detoxification of free radicals. The use of antioxidant rich food or antioxidant food supplements became immensely popular since many diseases have been associated with oxidative stress[20].

The leaves of *W. volubilis* are used traditionally in AndhraPradesh, in a paste form in the treatment of fissures in the feet and in rheumatic pain[21] an ointment known as Hemajeevanti prepared from the leaves was found to be effective in the treatment of wounds, tinea pedis, scabies, and in plantar psoriasis[22].

The leaves are applied to boils and abscesses to promote suppuration[23]. *W. volubilis* is distributed throughout the hotter parts of India, Taiwan, Cambodia, Nepal and Sri Lanka[24].

The goal of this study was to investigate the effects of aluminium exposure on liver tissue. The potential protective effect of *Wattakaka volubilis* on tissue

antioxidant & lipid profile against aluminium sulphate exposed rats.

MATERIALS AND METHODS

Plant material

The leaves of *Wattakaka volubilis* were collected from Trichirappalli. The plant material was taxonomically identified by Dr. JohnBritto Rabinet Herbanium. St. Joseph's college, Trichy.

Preparation of extract

The leaves of *Wattakaka volubilis* were dried in shady condition and powdered. The 200gm of powdered material was dissolved with 250ml of 95% methanol and extract was prepared using soxhlet apparatus for 48hr. The extract was filtered and concentrated in rotatory evaporator at 35-40°C under reduced pressure (yield: 28.5% w/w) and was stored in refrigerated condition for further use.

Drugs and chemicals

Aluminium sulphate and Silymarin were purchased from Sigma-Aldrich chemical company (St. Lousis mo, USA). The diagnostic kits required for enzymatic assays were purchased from Span Diagnostics.

Experimental animals

Adult male Wistar Albino rats weighing 250-350g were used for the present investigation. They were housed in a clean polypropylene cage and maintained under standard laboratory conditions(temperature 25±2°C with dark/light cycle 12/12h). They were fed with standard pellet diet (Hindustan lever, Kolkata, india) and water ad libitum. The animals were acclimatized to laboratory conditions for one month to experiment. All procedures described were reviewed and approved by the animal ethics committee, IAEC No/232 Sastra Uuniversity, Tanjavur, Tamil Nadu, India.

Experimental design

The animals were divided into 7 groups consisting of 6 animals in each group. Group I rats received saline (1ml/kg b.wt), Group–II rats administered twice with Aluminium sulphate (50mg/kg/day) dissolved in (1ml/kg b.wt) saline will be injected intraperitoneally double dose per week to induce hepatotoxicity. Group III, IV and V will be administered with Aluminium sulphate same procedure like Group II and also treated with MEWV (100mg/kg/b.w) (200mg/kg/b.w), (400mg/kg/b.w) dissolved in corn oil (1ml/kg b.wt) orally for 30days. Group VI, the hepatotoxicity induced rats were treated with silymarin (25mg/kg/b.w) dissolved in corn oil (w/v) orally for 30 days. Group VII rats were treated with MEWV alone (200mg/kg/b.w) dissolved in corn oil (1ml/kg b.wt) orally for 30days. The body weights of rats of each group were measured before the experimental trial and 30 days after the MEWV treatment. Liver weight of all rats was measured after the sacrifice.

Animals were sacrificed by injecting with sodium pentabarbitone and blood was collected in plain and heparinized tubes immediately after sacrifice for biochemical assays. Liver was removed and washed with saline. Blood samples centrifuged for 10min at 2500 rpm and the serum separated stored at 4°C until further investigations. Total cholesterol[25], Phospolipids[26], Free fetty acids[27], Triglycerides[28] Low density lipo protein (LDL)[29], Very low density lipo protein (VLDL)[30], High density lipo protein (HDL)[31] were analysed.

Antioxidant enzymes were measured by Catalase(CAT)[32], Super oxide dismutase (SOD)[33], Lipid peroxidation (LPO)[34], Reduced glutathione (GSH)[35], Glutathione peroxidase (GPx)[36] and Glutathione reductase (GR)[37] Glutathione S-transferase (GST)[38] were analysed in the normal, aluminium sulphate induced and drug treated rats.

The hepatoprotective action of MEWV was determined in aluminium sulphate induced hepatotoxic models by various biochemical parameters, lipid profile, lipoprotein and antioxidant enzymes.

Statistical analysis

The data were statistically analysed and all values were expressed as mean ± S.E.M. The data were also analyzed by one way ANOVA followed by Dunnet's t3-test. $P< 0.05$, $P< 0.01$, $P< 0.001$ was considered significant.

RESULTS AND DISCUSSION

The present study, $Al_2(SO_4)_3$ was employed as toxic agent and the protective effect of methanol extract of wattakaka volubilis against the aluminium sulphate induced hepatotoxicity was studied. The extent of toxicity was estimated by lipid profile, and lipo protein & antioxidant enzymes. The antioxidative and free radical scavenging activities of many substances have been assessed and many substances that possess anti hepatotoxic activity show strong antioxidative activity[39]. Aluminium sulphate is a widely used to induce toxic liver injury in a range of laboratory animals. The methanolic leaf extract of *wattakaka volubilis* and silymarin treated rats showed a significant decrease in the content of lipid profiles, when compared with hepatic rats.

Table-1 & fig:1 shows lipid profiles following Aluminium sulphate treatment and control rats. The concentration of lipid was found to be significantly reduced in aluminium treated rats.

The reduction of lipid may be correlate with the aluminium sulphate induced increased lipid peroxidation. It has been reported that aluminium promotes the production of free radicals resulting in Al-Fe interdependence reaction[40]. Total cholesterol and triglycerides, free fatty acids, were found to be elevated in aluminium sulphate treated rats when compared with normal rats. The increase in serum TG may be due to hypo activity of lipoprotein lipase in blood vessels which breaks up TG. High serum cholesterol level may results from the hepatic dysfunction. The levels of lipoprotein,

(LDL, HDL, VLDL, HDL:LDL, TC:HDL) in control and experimental animals were investigated (Table-2&fig: 2). Aluminium sulphate induced rats showed significantly increased serum lipid profiles expect HDL when compared with normal rats. The silymarin and methanol extract of *W.Volubilis* leaf treated rats showed a significant decrease in the content of lipid profiles when compared with aluminium sulphate induced rats. Similarly HDL level decreased in AL_2SO_4 induced in rats when compared to normal rats. On administration of methanol extract of *W.Volubilis* leaf and silymarin to the hepatic rats. HDL level was found to be restored to normal.

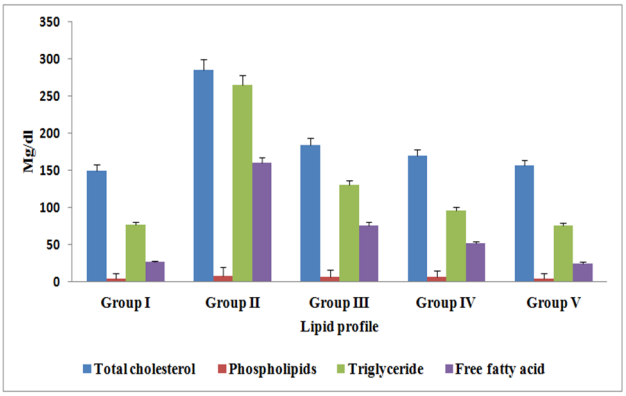

Figure 1: Effect on MEWV of Lipid profile in control and experimental animals.

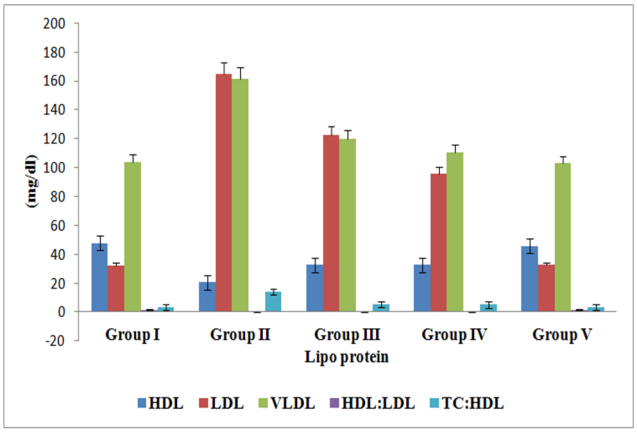

Figure 2: Effect on MEWV of Lipoproteins in control and experimental animals.

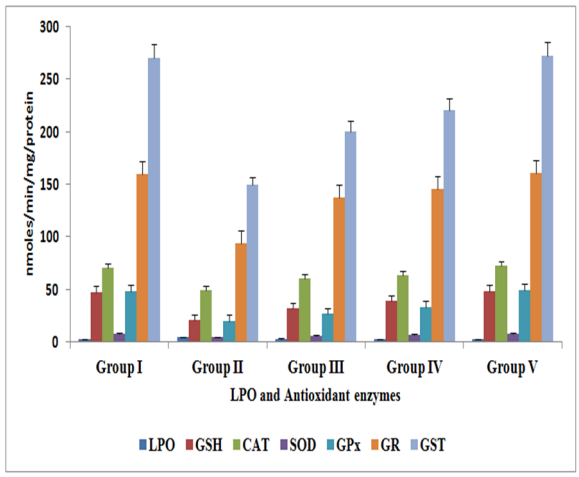

Figure 3: Effect on MEWV of LPO and Antioxidant enzymes in control and experimental animals.

The results (Table 3 and fig 3) showed increased lipid peroxidation (LPO) of aluminium sulphate induced in rats. Although biological function of Al is not understood very well[41] it has been reported that aluminium exposure can increase lipid peroxidation rates[42,43]. Effects of Al on lipid proxidation in various tissues such as liver, kidney, testis and brain of different animals were investigated and aluminium increased the rate of lipid peroxidation in some studies[44,45] while these changes were not observed in some studies[46,47]. In the present study, an increase in the levels of LPO was found and these levels were significantly reduced after supplementation of the methanol extract of *Wattakaka volubilis* leaf and silymarin. The levels of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), reduced glutathione (GSH), and glutathione reductase (GR), were significantly ($p<0.001$) reduced in aluminium sulphate induced rats. These adverse changes were reversed to near normal values in methanol extract of *W.*volubilis leaf treated. It is well known that SOD, CAT and GPx play an important role as protective enzymes against free radical formation in tissues. The present study indicates the reduction in the activity of SOD, CAT, GPx, GSH and GR in aluminium sulphate induced in rats. These results reveal the protective role of plant extract in decreasing lipid peroxidation and by normalizing antioxidant system.

Table 1: Effect of MEWV on Lipid profile in control and experimental rats

Groups	Total Cholesterol	Phospholipids	Triglyceride	FFA
Control	149.8±10.6	4.63±0.31	76.6±2.6	26.65±1.3
Aluminium sulphate (50 mg/kg/b.w)	284.4±16.5*	7.85±0.28*	264.3±10.8*	159.5±10.5*
$Al_2(SO_4)_3$+MEWV (200 mg/kg/b.w)	183.6±11.1$^{\#}$	6.26±0.43^{a}	130.1±9.4$^{\#}$	76.9±2.1$^{\#}$
$Al_2(SO_4)_3$+Silymarin (25 mg/kg/b.w)	169.2±13.5$^{\#}$	6.07±0.41$^{\#}$	95.4±5.3$^{\#}$	51.5±1.7$^{\#}$
MEWV (200mg/kg/b.wt)	156.3±14.6	4.76±0.29	75.3±4.9	25.06±2.3

Results are expressed as mean ± S.E.M, n = 6. *P < 0.05, statistically significant as compared with control rats and ^{a}P < 0.05 statistically significant as compared with $Al_2(SO_4)_3$ induced group.

Table 2: Effect of MEWV on Lipoprotein in $Al_2(SO_4)_3$ induced rats.

Groups	HDL	LDL	VLDL	HDL:LDL	TC:HDL
Control	47.8±0.91	32.28±0.94	104±2.71	1.44±0.40	3.05±0.46
Aluminium sulphate (50 mg/kg/b.w)	20.49±0.74*	164.62±1.55*	161.2±2.81*	0.11±0.02*	13.99±0.25*
$Al_2(SO_4)_3$+MEWV(200 mg/kg/b.w)	32.47±2.6[a]	122.2±1.53[a]	120.1±1.84[a]	0.28±0.10[a]	5.09±0.76[a]
$Al_2(SO_4)_3$+Silymarin (25 mg/kg/b.w)	32.61±1.08[a]	95.84±1.00[a]	110.5±1.31[a]	0.33±0.10[a]	5.01±0.74[a]
MEWV (200mg/kg/b.wt)	45.65±1.27	32.5±0.54	102.8±2.04	1.38±0.44	3.1±0.42

Results are expressed as mean ± S.E.M, n = 6. *P < 0.05, statistically significant as compared with control rats and [a]P < 0.05 statistically significant as compared with $Al_2(SO_4)_3$ induced group.

Table 3: Effect of MEWV on Lipid peroxidation & Antioxidants levels in $Al_2(SO_4)_3$ induced rats

Groups	LPO	GSH	CAT	SOD	GPx	GR	GST
Control	2.31±0.16	47.6±1.9	70.50±4.6	7.41±0.15	48.6±2.5	159.4±9.5	269.5±14.7
Aluminium sulphate (50 mg/kg/b.w)	4.32±0.18*	20.6±0.11*	48.7±2.6*	4.3±0.18*	19.8±1.4*	94.1±7.4*	149.5±8.6*
$Al_2(SO_4)_3$+MEWV (200 mg/kg/b.w)	3.04±0.21[a]	31.6±1.2[a]	60.4±4.4[a]	6.1±0.53[a]	26.4±2.7[a]	136.9±9.8[a]	200.3±10.5[a]
$Al_2(SO_4)_3$+Silymarin (25 mg/kg/b.w)	2.57±0.19[a]	38.9±2.6[a]	63.50±1.7[a]	6.65±0.48[a]	33.1±1.5[a]	145.3±10.1[a]	220.6±15.8[a]
MEWV (200mg/kg/b.w)	2.27±0.19	48.5±1.6	72.4±3.6	7.49±0.58	49.3±0.32	161.0±10.9	271.9±12.4

Results are expressed as mean ± S.E.M, n = 6. *P < 0.05, statistically significant as compared with control rats and [a]P < 0.05 statistically significant as compared with $Al_2(SO_4)_3$ induced group.

CONCLUSION

It is concluded that, medicinal plants have been reported to possess antihyperlipidemic activity *Wattakaka volubilis* leaf is gaining much importance in liver toxic control as it has been used as a traditional medicine for hepatotoxicity. In the present study the MEWV dose dependently offered potential hepato protection against $AL_2(SO_4)_3$. Induced hepatic damage, normalizing, lipid profile, lipoprotein, antioxidant defense mechanism. Further detailed investigations on this W. volubilis are needed in order to identify and isolate the hepatoprotective components in the extract and to justify its use in the treatment of liver disorders. Finally, the education of the public and medical profession is needed to increase awareness of the potential toxic effects of aluminium sulphate.

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