© by PSP Volume 31– No. 08/2022 pages 7902-7909 Fresenius Environmental Bulletin

COMPARATIVE STUDY BETWEEN THE TOXICITY OF ALUMINIUM CHLORIDE AND MERCURIC CHLORIDE ON BIOCHEMICAL MARKERS AND LIPID PROFILES IN WISTAR RATS

Sayah Sarra[1,*], Khaldi Fadila[1], Araar Samia[1], Chaib Sakina[2], Gheid Abdelhak[1]

[1]Laboratory of Sciences and Technology of Water and Environment, Department of Biology, Faculty of Life and Natural Sciences, Mohamed Cherif Messaadia University, Souk Ahras, 41000, Algeria
[2]Laboratory of Environmental Biosurveillance (LBSE), Department of Biology, Badji Mokhtar University, BP 12 Sidi Amar, 23000 Annaba, Algeria

ABSTRACT

This study was designed to compare the between the toxic of aluminum chloride ($AlCl_3$) and mercuric chloride ($HgCl_2$) on biochemical markers of liver function, and lipid profiles in Wistar rats. Forty-two male albino Wistar rats were equally divided into three main groups as untreated control (n= 6) group and two treated (n = 6) groups which then were subdivided each into three different subgroups depending on the metal type and doses, namely $AlCl_3$ at doses 7.6, 12.66, and 38 mg/kg body weight (bw), and $HgCl_2$ at doses 0.1, 0.2, and 0.4 mg/kg (bw). Treatments were given to rats orally for 28 days. Results showed a decrease in body weight, and an increase in relative and absolute liver weights, in addition to a significant increase in the levels of serum glucose, bilirubin (total and direct), cholesterol and triglycerides, and the enzymatic activities of transaminases (TGO, TGP) and alkaline phosphatase (PAL), and conversely a decreased level of total proteins in Al and Hg treated animals compared to the controls. The biochemical alterations were supported by the histopathological evaluation of the liver, showing vascular congestion, sinusoid disintegration, centrilobular vein disintegration, and inflammatory cell infiltration. In conclusion, $AlCl_3$ and $HgCl_2$ have induced liver dysfunction, and $HgCl_2$ was proved to be a very toxic metal compared to $AlCl_3$.

KEYWORDS:
Subacute toxicity, Hepatotoxicity, Rats, $AlCl_3$, $HgCl_2$

INTRODUCTION

Heavy metals are pollutants generated by human activity and can induce serious toxicological effects on plants, and the health of humans consuming common contaminated food products [1, 2].

Heavy metals (e.g. mercury and aluminum) of which some are carcinogens, and all even at low concentration levels can cause harmful effects, as well as they, tend to accumulate in the food chain [3].

The general population is exposed to metals via consumption of contaminated water and foodstuffs, via inhalation of contaminated air, or direct skin contact, leading consequently to adverse health effects [4].

Aluminum (Al) is a ubiquitous abundant heavy metal in the earth's crust [5]. Its typical physicochemical properties make it a widely used metal in building, transportation systems (vehicles, planes, trains, etc.), food packaging, kitchen utensils, pyrotechnics, personal care products pose, and medicines including vaccines as adjuvants or active ingredients in antacids, etc... [6, 7]. As a result, humans face a considerable toxic risk likely leading to complications and disturbances of vital functions and neurodegenerative diseases [8, 9], in addition to metal bioaccumulation in various body organs, including bones, liver, kidneys, brain, etc. [10].

Moreover, mercury (Hg) is a highly toxic metal causing a range of adverse health effects, including neurological, renal, respiratory, immune, dermatological, reproductive, and developmental effects [11]. It enters the human body primarily through the digestive and respiratory systems, then is transported through the bloodstream to soft target organs (liver, kidneys, lungs, and brain) where it highly accumulates [12]. Additionally, mercury alters cell biology by interfering with several metabolic pathways and physiological processes, and it was reported even at low doses it can induce adverse effects on kidney function and may lead to liver necrosis [13].

Overall, the toxicity of heavy metals, including Al and Hg involves the induction of oxidative stress via the generation of reactive oxygen species, leading to oxidative organ injuries [3]. As reported [14], the liver is the main organ in the body for eliminating toxic waste because it has an enzymatic system involved in the detoxification process and the neutralization of all toxic compounds. Since no comparative study investigating the toxic effects of Al and

Hg on liver function is available, the present study was therefore undertaken to compare the toxic effects of $AlCl_3$ and $HgCl_2$ on liver function biochemical markers and lipid profiles in Wistar rats.

MATERIALS AND METHODS

Biological materials. Forty-two male albino Wistar rats aged eight weeks, and weighing between 180 and 220 g were obtained from the Pasteur Institute of Algiers, Algeria. The rats were kept in plastic cages in an animal house at a temperature of 22 +/- 2° C and a standard relative humidity with a 12-h light/dark cycle. The animals had free access to water and food diet prepared according to [15]. The Animal Care Committee and the Ethics Committee of our Institution authorized all experimental procedures.

Chemical materials. Aluminum chloride Anhydrous form (III) ($AlCl_3$. 6 H_20) and mercury chloride ($HgCl_2$) were purchased from Sigma Aldrich Company (St. Louis, MO, USA).

Experimental protocols. The rats were divided into three main experimental groups (6 rats/group), including two treated groups and the control untreated group received drinking water by gavage. The two treated groups were subdivided each into three subgroups received aluminum chloride ($AlCl_3$) (mg/kg body weight (bw)) in doses corresponding to 1/50, 1/30 and 1/10 of the LD50, respectively, 7.6, 12.66, and 38 mg/kg, and mercury chloride ($HgCl_2$) in doses corresponding to 1/10, 2/10 and 4/10 of the LD50, respectively 0.1, 0.2, and 0.4 mg/kg (bw).

$AlCl_3$ and $HgCl_2$ solutions were given orally to rats as 1ml of each for 28 consecutive days. After the treatment period, animals were sacrificed by decapitation to avoid stress effect, the collected blood samples into dry tubes were centrifuged at 3000 rpm for 10 minutes, and the resulting serum samples were used for the biochemical analyses. In addition, the liver samples of each animal from control and treated groups were immediately removed and rinsed in a 0.9% sodium chloride (NaCl) solution, then weighed and fixed in formalin for histopathological evaluation.

Biochemical analysis. The biochemical parameters, including glucose, cholesterol, triglycerides, total proteins, total bilirubin (BT), direct bilirubin, transaminases (TGO and TGP), alkaline phosphatase ALP were spectrophotometrically evaluated by the enzymatic colorimetric method (Mindray BA-88A).

Histopathological evaluation. Liver fragments from each experimental group were fixed in formalin solution for 24 hours, and then subjected to histological procedures as previously described [16]. In brief, liver sections were dehydrated using a graded series of ethanol and then embedded in paraffin wax. Liver paraffin sections were sliced into 5µm thick and stained with hematoxylin and eosin. The histological slides were examined under a light microscope (Optika B-290).

Statistical analysis. Results are displayed as mean ± SE of the mean. The differences between the experimental groups were tested by one-way ANOVA (analysis of variance) followed by a Student's t-test, using SPSS software (Version 20.23). The difference is considered significant at $P < 0.05$.

RESULTS

Physiological observations. As indicated in Table 1, the body weight significantly reduced ($p<0.05$) in 0.2 and 0,4 mg/kg bw $HgCl_2$ treated animals compared to controls, meanwhile $AlCl_3$ treatment did not induce any significant variation in body weight. Further, the absolute and relative liver weights increased significantly ($p<0.05$) in rats treated with $AlCl_3$ at 12 .66 mg/kg bw, but $AlCl_3$ at 38mg/Kg bw induced a highly significant ($P \leq 0.01$) increase in the absolute liver weight, and a very highly significant ($P<0.001$) increase in relative liver weight compared with the control group. While, 0,4mg/kg bw $HgCl_2$ treatment caused a very highly significant increase (P<0, 001) in the absolute and relative weights of the liver, but 0,2mg/kg bw $HgCl_2$ treated group revealed a highly significant ($P\leq0.01$) increase in liver weights. On the other hand, the low dose of 0.1 mg/Kg bw of $HgCl_2$ induced a significant ($p< 0.05$) increase in the absolute liver weight and a highly significant ($P \leq 0.01$) increase in the relative liver weight as compared with control rats.

Biochemical evaluations. The serum glucose level increased, significantly ($p<0.05$), highly significantly ($P \leq 0.01$) and very highly significantly ($P<0.001$) respectively in 0.1mg/Kg bw, 0,2mg/kg bw and 0,4mg/kg bw $HgCl_2$ treated rats compared to controls. Comparatively, a highly significant ($P \leq 0.01$), and significant ($p< 0.05$) increase in the serum glucose level was noticed, respectively in 38mg/Kg bw and 12.66 mg/kg bw $AlCl_3$ treated rats, along with no significant change in 7.6 mg/kg bw $AlCl_3$ treated rats when compared with control rats.

Regarding the liver enzymatic activity, both chemicals induced marked elevation in transaminases (TGO and TGP) and ALP activity compared with control rats. Here, 0.1mg/Kg bw, 0.2mg/Kg bw and 0.4mg/Kg bw of $HgCl_2$ treated animals compared to controls caused, respectively a significant ($P<0.05$), a highly significant ($P<0.01$), and a very highly significant ($P<0.001$) increase in the activity

TABLE 1
Bodyweight and liver weights (absolute and relative) in control and treated rats with $AlCl_3$ and $HgCl_2$.

Parameters	Treatments						
	Control	$ALCL_3D1$	$ALCL_3D2$	$ALCL_3D3$	$HgCL_2D1$	$HgCL_2D2$	$HgCL_2D3$
Initial weight (g)	239,67±9,93	238,50±8,26	238,83±8,01	239,83±6,49	241,17±8,75	239,50±5,85	240,67±6,08
Final weight (g)	250,17±12,89	244±4,77	239,17±5,84	239,50±4,32	238,83±4,53	236,17±6,36*	235,50±4,59*
Absolute liver weight (g)	5,55±0,16	5,75±0,33	6,09±0,46*	6,40±0,52**	6,15±0,55*	6,63±0,65**	7,54±0,49***
Relative liver weight (g/100 g b.w.)	2,22±0,11	2,35±0,12	2,55±0,23*	2,67±0,17***	2,57±0,21**	2,81±0,33**	3,20±0,23***

*p < 0,05; ***p < 0,001: Significant difference compared to the control group.

of these enzymes when compared with controls. In parallel, the enzymatic activity was, respectively increased significantly ($P \leq 0.05$), highly significantly ($p<0.01$), and not significantly in 12.66 mg/kg bw, 38mg/Kg bw, and 7.6 mg/kg bw $AlCl_3$ treated rats compared to controls (Table 2).

Moreover, the serum concentration of bilirubin (direct and total bilirubin) was increased significantly ($p < 0.05$), highly significantly ($p < 0.01$), and very highly significantly ($p < 0.001$) respectively in 0,1mg/kg bw, 0,2mg/kg bw and 0,4mg/kg bw $HgCl_2$ treated animals compared to controls. This parameter was also increased significantly ($p<0.05$) and highly significantly ($P \leq 0.01$) respectively in 12.66 mg/kg bw and 38mg/kg bw $AlCl_3$ treated groups compared with the control group, since the low dose of $AlCl_3$ (7,6mg/kg bw) did not cause significant change.

In addition, the level of the serum total proteins was decreased significantly ($p<0.05$), highly significantly ($P<0.01$) and very significantly ($P<0.001$), respectively in 0,1mg/kg bw, 0,2mg/kg bw and 0,4mg/kg bw $HgCl_2$ treated groups compared with control group. By comparison, the serum concentration of this parameter was not significantly changed, significantly ($p< 0.05$) and highly significantly decreased in 7.6 mg /kg bw, 12.6 mg /kg bw and 38 mg /kg bw $AlCl_3$ treated rats compared with controls (Table 2).

Lipid profiles. As indicated in Table 3, subacute oral exposure of $AlCl_3$ and $HgCl_2$ for 28 days induced an increase in cholesterol and triglyceride levels compared to the control group. Precisely, these parameters were highly significantly ($p < 0.01$) and very highly significantly ($p < 0.001$) increased respectively in 0,2mg/kg bw and 0,4mg/kg bw $HgCl_2$ when compared with control group, while 0,1mg/kg bw $HgCl_2$ showed a significant decrease in these parameters as compared with those of

TABLE 2
Effect of $AlCl_3$ and $HgCl_2$ on hepatic biochemical markers.

Parameters	Treatments						
	Control	$ALCL_3D1$	$ALCL_3D2$	$ALCL_3D3$	$HgCL_2D1$	$HgCL_2D2$	$HgCL_2D3$
Glucose (g/l)	0,78±0,026	0,81±0,023	0,82±0,018*	0,85±0,030**	0,82±0,027*	0,86±0,046**	0,95±0,047***
ASAT (U/L)	114,6±9,65	122,28±5,28	127,11±5,45*	134,06±6,09**	126,9±5,37*	132,7±4,22**	148,4±3,67***
ALAT (U/L)	44,38±2,90	47,51±3,87	48,5±2,57*	51±3,73**	48,71±3,60*	53,33±4,54**	58,20±5,49***
ALP (U/L)	134,31±4,10	139,28±5,33	141,37±4,42*	144,52±5,43**	140,54±3,45*	143,53±3,62**	152,44±5,13***
TB (mg/L)	1,06±0,043	1,09±0,041	1,11±0,018*	1,18±0,077**	1,12±0,028*	1,29±0,15**	1,60±0,29***
DB (mg/l)	0,39±0,036	0,41±0,030	0,44±±0,030*	0,51±0,063**	0,44±0,038*	0,49±0,052**	0,57±0,045***
Total protein (g/L)	84,34±3,35	82,12±1,64	80,45±1,30*	76,21±3,37**	80,33±2,50*	75,22±4,23**	67,16±2,77***

TB: total bilirubin; DB: direct bilirubin; ASAT: aspartate aminotransferase; ALAT: alanine aminotransferase; ALP: alkaline phosphatase.
*p < 0,05; **p < 0,01; ***p < 0,001: Significant difference compared to the control group

TABLE 3
Effect of $AlCl_3$ and $HgCl_2$ on the lipid profiles.

Parameters	Treatments						
	Control	$ALCL_3D1$	$ALCL_3D2$	$ALCL_3D3$	$HgCL_2D1$	$HgCL_2D2$	$HgCL_2D3$
Cholesterol (g/l)	0,71±0,023	0,72±0,059	0,76±0,050*	0,81±0,075**	0,75±0,038*	0,77±0,045**	0,88±0,06***
Triglycerides (g/l)	0,64±0,033	0,67±0,037	0,71±0,052*	0,76±0,055**	0,72±0,07*	0,74±0,044**	0,83±0,050***

*p < 0,05; **p < 0,01; ***p < 0,001: Significant difference compared to the control group

7,6mg/kg bw $AlCl_3$ treated rats, showing no significant changes. Further, the serum levels of lipid parameters (cholesterol and triglycerides) showed a significant ($P \leq 0.05$) and a highly significant ($P \leq 0.01$) increase, respectively in 12.66 mg/kg bw and 38 mg/kg bw $AlCl_3$ treated rats compared to those in controls.

Histopathological observations. Microscopic observation of liver histological sections from control rats showed normal structural architecture of hepatocytes; rounded or hexagonal hepatocyte cells separated by central veins (Figure 1A).

The administration of $AlCl_3$ at a dose of 7.6 mg/kg bw caused dilation of the centrilobular vein and vascular congestion (Figure 1B), while 0.2 mg/kg $HgCl_2$ treatment-induced various pathological alterations in the rat liver, evidenced by vascular congestion and inflammatory infiltration (Figure 2B).

Moreover, 12.66 mg/kg bw $AlCl_3$ treatment caused dilation of the centrilobular vein, vascular congestion (Figure 1C), and similarly, 0.2 mg/kg of $HgCl_2$ led to significant vascular congestion, dilation of Sinusoids and inflammatory infiltration (Figure 2C). Also, 38 mg/kg bw $AlCl_3$ treatment caused vascular congestion, dilation of the centrilobular vein, dilation of sinusoids, slight infiltration (Figure 1D).

However, the dose of 0.4 mg/Kg bw of $HgCl_2$ caused very significant vascular congestion, dilation of the centrilobular vein and dilation of sinusoids.

DISCUSSION

In this study, we evaluated firstly the changes in rat body weight following the metals treatments. This physiological parameter is a valuable indicator in assessing the toxicological risks in chemicals exposed to human and experimental animals [17].

In our experimental conditions, results showed a marked decline in body weight in $HgCl_2$ exposed rats compared to controls, and this is in line with that previously reported [18]. This effect may be explained by the action of mercury on the transfer of nutrients (amino acids, glucose, and essential minerals, including selenium, zinc, magnesium, iron, etc.) through the bloodstream, and as a result, the absorption of food by the body can be weak.

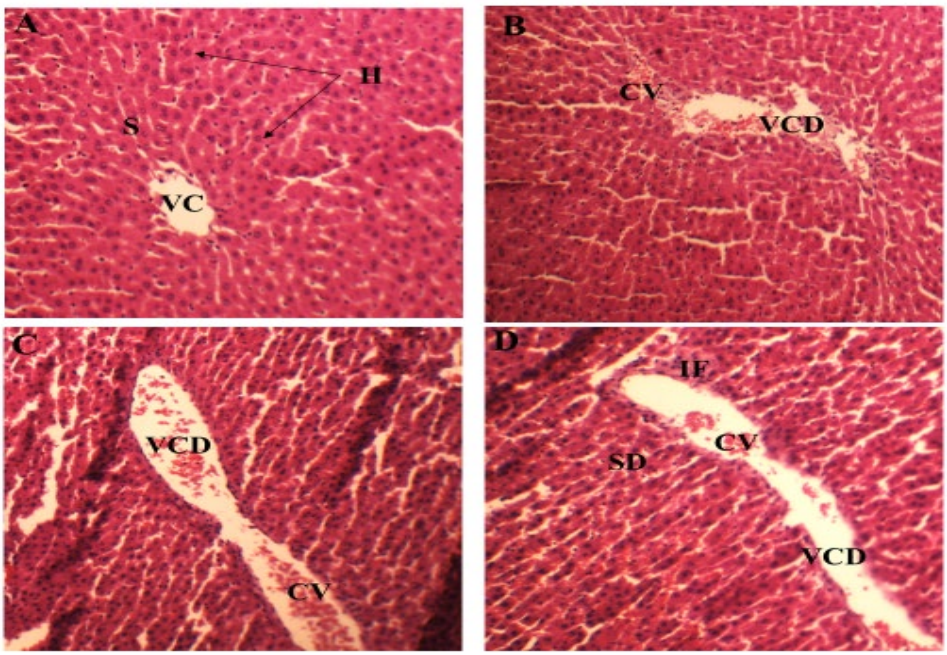

FIGURE 1
Light microscopic observation of the liver stained by hematoxylin and eosin (HE) in control and $AlCl_3$ treated rats.

A): Control rats, B): AlCl3 7,6mg/kg; C): AlCl3 12,66mg/kg; D): AlCl3 38mg/kg for 28 days (G x 400).
H: Hepatocyte, CV: Centrilobular vein, S: Sinusoids, SD: Dilated sinusoids, VCD: Dilated centrilobular vein, CV: Vascular congestion, IF: Slight infiltration.

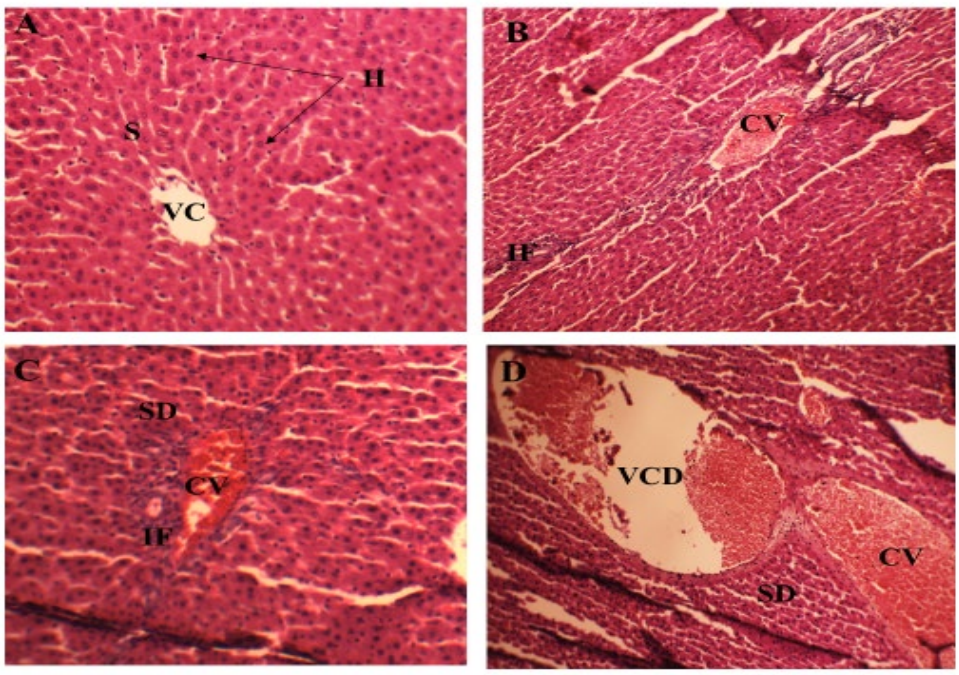

FIGURE 2
Light microscopic observation of the liver stained by hematoxylin and eosin (HE) in control (A) and $HgCl_2$ treated rats (B). B): $HgCl_2$ 0,1mg/kg (bw); C): $HgCl_2$ 0,2mg/kg (bw); D): $HgCl_2$ 0,4mg/kg (bw) for 28 days (G x 400).
H: Hepatocyte, CV: Centrilobular vein, S: Sinusoids, SD: Dilated sinusoids, VCD: Dilated centrilobular vein, CV: Vascular congestion, IF: Slight infiltration.

Unlike this result, $AlCl_3$ did not cause marked variations in rat body weight, and this disagrees with those obtained by Buraimoh and Ojo [19] proving that the exposure to increasing doses of $AlCl_3$ (475 to 1900 mg/kg) caused significant body weight loss in Wistar rats. On top of that, a reduction in water and food intake and transient diarrhea resulted in decreased final body weight was reported in rats receiving 80 mg/l $AlCl_3$ for 3 months [20].

As reported Simons et al [21], the increase in absolute or relative animal organ weights is a valuable indicator of toxicity of tested chemicals. In this context, our results revealed a significant increase in the absolute and relative liver weights in $AlCl_3$ and $HgCl_2$ exposed rats compared with controls. This is somehow related to the accumulation of these metals in the liver as their main target organ [22].

Furthermore, the liver enzymatic activity of transaminases (TGO, TGP), and alkaline phosphatase (ALP) were significantly increased in $AlCl_3$ and $HgCl_2$ treated rats when compared with control rats. These enzymes are the main markers of liver toxic injuries [23]. The hepatic injuries associated with $AlCl_3$ – induced hepatotoxicity in rats lead to a significant increase in the enzymatic activity of the liver enzyme markers, including transaminases (GPT/TGO) and alkaline phosphatase (ALP) [24, 25, 26, 27, 28]. Similarly, the significant increase in the enzymatic activity of TGP, TGO, and ALP observed in $HgCl_2$ – treated rats may be explained by the alterations in the cell membrane permeability resulting in the leakage of cell proteins, including enzymes from the liver tissue to the bloodstream [13].

Results showed also an increase in the concentration of bilirubin (total and direct) in rats treated with $AlCl_3$ and $HgCl_2$. As reported, the increased level of bilirubin in chemicals intoxicated rats indicates liver dysfunction, and accordingly, [29,30] have proved this finding in their studies. The hyperbilirubinemia associated with the toxicity of various chemicals is an indicator of liver injuries [31].

On the other hand, the level of serum total proteins was reduced in $AlCl_3$ and $HgCl_2$ treated rats compared with controls. This is likely due to the decrease in the protein synthesis process, as well as the strong binding of mercury with the protein thiol groups (SH, OH), and the free radicals generated by this metalloid, make proteins have desaturated and fragmented structure, or lose their primary and secondary structures [32].

Similar results have been reported in some studies investigating the toxicity of Ni in mice [33, 34], and suggesting that nickel can modify protein and amino acid metabolism and their synthesis in the liver.

In this study, the hyperglycemia observed in $AlCl_3$ and $HgCl_2$ treated rats compared with controls is likely due to the inhibition of insulin production by the islets of Langerhans or to the incapacity of using glucose by body cells [35].

Additionally, the Al intoxicated rats may result in disruption of carbohydrate metabolism through increased hepatic glycogen breakdown, which is possibly due to increased adrenocorticotropic hormones and glucagon and/or reduced insulin activity [36].

Regarding the effect of treatments on lipid profiles, our findings showed a significant increase in the serum concentration of cholesterol and triglycerides in rats intoxicated with $AlCl_3$ and $HgCl_2$ compared to control rats. This increase may be the result of the intense degradation of lipids in the adipose tissues in the body [37]. In addition, the observed elevation of serum levels of cholesterol and triglycerides may indicate a possible oxidative lipid peroxidation of the cell membrane [38,39].

The adverse biochemical alterations caused by $AlCl_3$ and $HgCl_2$ toxicity were supported by the liver histopathological observations, indicating vascular congestion, the disintegration of sinusoids, disintegration centrilobular vein, infiltration of inflammatory cells, congested sinusoids and blood vessels, cellular degeneration with nuclear pyknosis, and the presence of necrotic areas. These histological damages were similarly reported in the study by El-Sayed et al [40] investigating the hepatotoxicity of $AlCl_3$ in mice.

CONCLUSION

The present study demonstrated that exposure of rats to aluminum chloride and mercury chloride-induced a hepatotoxicity injury characterized by marked liver biochemical alterations and histological damages. These changes were greater for $HgCl_2$ than those for $AlCl_3$, and this is evidenced by the lower LD50 value of $HgCl_2$ than that of $AlCl_3$.

REFERENCES

[1] Durak, D., Kalender, S., Uzun, F. G., Demir, F. and Kalender, Y. (2010) Mercury chloride-induced oxidative stress and the protective effect of vitamins C and E in humanerythrocytes in vitro. Afr. J. Biotechnol. 9 (4), 488–495.

[2] Amir, W., Jahanzaib, A., Farhat, I., Ashif, S., Zahid, M. and Ghulam. M. (2014) Pollution Status of Pakistan: A Retrospective Review on Heavy Metal Contamination of Water, Soil, and Vegetables. BioMed. Research International. 2014, 29 pp.

[3] Garcia-Nino, W.R. and Pedraza-Chaverri, J. (2014) Protective effect of curcumin againstheavy metals-induced liver damage. Food Chem. Toxicol. 69,182–201.

[4] Alissa, E. and Ferns, G. (2011) Heavy metal poisoning and cardiovascular disease. Journal of Toxicology. 2011, 1–21.

[5] Ferguson, G. (2018) Systematic review of occupational aluminum Exposure and adverse health conditions. Intrinsik .2018, 1-71.

[6] WHO (World Health Organization). (2010) Aluminum in drinking water: Background document for development of WHO guidelines for drinking-water quality.

[7] Taïr, K., Kharoubi, O., Taïr, O. A., Hellal, N., Benyettou, I. and Aoues, A. (2016) Aluminium-induced acute neurotoxicity in rats: Treatment with aqueous extract of Arthrophytum (Hammada scoparia). Journal of Acute Disease. 5(6), 470-482.

[8] Zatta, P., Zambenedetti, P.T. and Milanese, M. (1999) Activation of monoamine oxidase type-B by aluminium in rat brain homogenate. Neuroreport.10(17), 3645–3648.

[9] Dave, K.R., Syal, A.R. and Katyare, S.S. (2002) Effect of long term aluminium feeding on kinetics attributes of tissue cholinesterases. Brain Research Bulletin. 58(2), 225-233.

[10] Abu-Taweel, G.M. and Al-Mutary, M.G. (2020) Pomegranate juice rescues developmental, neurobehavioral and biochemical disorders in aluminum chloridetreated male mice. Journal Of Trace Elements In Medicine And Biology. 63, 126655.

[11] Risher- john, F. and Amler- Sherlita, N. (2005) Mercury exposure: evaluation and intervention, the inappropriate use of chelating agents in diagnosis and treatment of putative mercury poisoning. Neurotoxicology.26(4), 691-699.

[12] Agarwal, R. and Behari, J. R. (2007) Effect of selenium pretreatment in chronic mercury intoxication in rats. Bulletin of Environmental Contamination and Toxicology.79(3), 306-310.

[13] Deepmala, J., Deepak, M., Srivastav, S., Sangeeta, S., Kumar, S.A. and Kumar, S.S. (2013) Protective effect of combined therapy with dithiothreitol, zinc and selenium protects acute mercury induced oxidative injury in rats. J. Trace Elem. Med. Biol. 27(3), 249-56.

[14] LeCluyse, E. L., Witek, R. P., Andersen, M.E. and Powers, M.J. (2012) Organotypic liver culture models: meeting current challenges in toxicity testing. Crit. Rev. Toxicol. 42(6), 501-48.

[15] Upreti, K.K., Das, M., Kumar, A. (1989) Biochemical toxicology of argemone oil. IV short-term oral feeding response in rats. Toxicology. 58(3), 285-298.

[16] Hould, R. (1984) Technical on histopathology and cytopathology. Ed Maloine. 19(21), 225 227. (In French).

[17] Yavasoglu, A., Karaaslan, M.A., Uyanikgil, Y., Sayim, F., Ates, U. and Yavasoglu, N.U. (2008) Toxic effects of anatoxin-a on testes and sperm counts of male mice. Exp. Toxicol. Pathol. 60(4-5),391-6.

[18] Necib, Y., Bahi, A., Zerizer, S., Abdennour, C. and Boulakoud, M.S. (2013i) Hepatoprotective role of sodium selenite against oxidative damage induced by mercuric chloride in rat albinos wistar. J. of Stress Physiol. and Biochem. 9(4), 230-240.

[19] Buraimoh, A.A. and Ojo, S.A. (2014) Effects of Aluminium chloride exposure on the body weight of Wistar rats. Ann. Bio Sci. 2(2), 66-73.

[20] Kowalczyk, E., Kopff, A., Kędziora, J., Błaszczyk, J., Kopff, M., Niedworok, J. and Fijałkowski P. (2004) Effect of Long-TermAluminium Chloride Intoxication on Selected Biochemical Parameters and Oxidative- -Antioxidative Balance in Experimental Animals. Polish Journal of Environmental Studies. 13(1), 41-43.

[21] Simons, J.E., Yang, R.S.H. and Berman, E. (1995). Evaluation of the nephrotoxicity of complex mixtures containing organic metals: advantages and desadvantages of the use of real-world complex mixtures. Environ. Health. Prespect. 103, 67-71.

[22] Agarwal, R., Kumar, R. and Behari, J. R. (2007) Mercury and lead content in fish species from the river Gomti, Lucknow, India, as biomarkers of contamination. Bulletin of Environmental Contamination and Toxicology. 78(2), 118-122.

[23] Burtis, C.A., Ashwood, E.R. and Bruns, D.E. (2008) Tietz Fundamentals of Clinical Chemistry. (6th Edition). Elsevier New Delhi. 322 – 329.

[24] Nehru, B., Anand, P. (2005) Oxidative damage following chronic aluminium exposure in adult and pup rat brains. Journal of Trace Elements in Medicine and Biology. 19(2-3), 203 – 208.

[25] Shati, A.A. and Alamri, S.A. (2010) Role of saffron (Crocus sativus L.) and honey syrup on aluminum induced hepatotoxicity. Saudi Med. J. 31(10), 1106-1113.

[26] Abdel-Wahab, W.M. (2012) Aluminium chloride-induced toxicity and oxidative stress in liver of male rats: Protection by melatonin. Life Science Journal. 9(4),1173 – 1181.

[27] Yakubu, O.E., Obot, A.C. and Dawoye, Y.(2016b) Effects of aqueous extract of Hymenocardia acida leaves on aluminium chloride-induced toxicity in male albino rats. Journal of Analytical and Pharmaceutical Research. 3(2), 00049.

[28] Bhadauria, M. (2012) Combined treatment of HEDTA and propolis prevents aluminum induced toxicity in rats. Food and Chemical Toxicology. 50(7), 2487-2495.

[29] Yousef, M.I. (2004) Aluminium-induced changes in hemato-biochemical parameters, lipid perocidation and enzyme activities of male rabbits: protective role of ascorbic acid. Toxicology. 199(1), 47-57.

[30] Ben Amara, I., Troudi, A., Garoui, E.M., Hakim, A., Boudawara, T., Zeghal, K.M. and Zeghal, N. (2011) Protective effects of selenium on methimazole nephrotoxicity in adult rats and their offspring. Experimental and Toxicologic Pathology. 63(6), 553- 561.

[31] Rana, S.V., Rekha, S. and Seema, V. (1996) Protective effects of few antioxidants on liver function in rats treated with cadmium and mercury. Ind. J. of Exp. Biol. 34, 177–179.

[32] Joshi, D., Mittal, D., Shrivastav, S., Shukla, S. and Srivastav, A. K. (2011) Combined effect of N-acetyl cysteine, zinc, and selenium against chronic dimethylmercury-induced oxidative stress: a biochemical and histopathological approach. Archives of Environmental Contamination and Toxicology. 61(4), 558-567.

[33] Pari, L. and Amudha, K. (2011) Hepatoprotective role of naringin on nickel-induced toxicity in male Wistar rats. European Journal of Pharmacology. 650(1), 364-370.

[34] Harris, R.M., Williams, T.D., Hodges, N.J. and Waring, R.H. (2011) Reactive oxygen species and oxidative DNA damage mediate the cytotoxicity of tungsten–nickel–cobalt alloys in vitro. Toxicology and Applied Pharmacology. 250(1), 19-28.

[35] Rao, M. V., Purohit, A. and Patel, T. (2010) Melatonin protection on mercury-exerted brain toxicity in the rat. Drug and Chemical Toxicology. 33(2), 209-216.

[36] Metwally, F. M. and Mazahr, M. S. (2007) Effect of aluminium on the levels of some essential elements in occupationally exposed workers. Arhiv za Higijenu Rada i Toksikologiju. 58(3), 305-311.

[37] Cempel, M., Janicka, K. (2002) Distribution of nickel, zinc, and copper in rat Organs after oral administration of nickel (II) chloride. Biological Trace Element Research. 90(1),215-226.

[38] Das, K. K., Das, S. N. and Gupta, S. D. (2001) Influence of ascorbic acid against nickel-induced hepatic lipid peroxidation in rats. Journal of Basic and Clinical Physiology and Pharmacology. 12(3), 187-196.

[39] Kubrak, C., Olson, K., Jha, N., Scrimger, R., Parliament, M., McCargar, L., and Baracos, V. E. (2013). Clinical determinants of weight loss in patients receiving radiation and chemoirradiation for head and neck cancer: a prospective longitudinal view. Head & Neck. 35(5), 695-703.

[40] El-Sayed, W.M., Al-Kahtani, M.A. and Abdel-Moneim, A.M. (2011) Prophylactic and therapeutic effects of taurine against aluminum-induced acute hepatotoxicity in mice. Journal of Hazardous Materials. 192, 880–886.

Received: **27.03.2022**
Accepted: **07.06.2022**

CORRESPONDING AUTHOR

Sayah Sarra
Laboratory of Sciences and Technology of Water and Environment,
Department of Biology, Faculty of Life and Natural Sciences,
Mohamed Cherif Messaadia University,
Souk Ahras 41000 – Algeria

e-mail: s.sayah@univ-soukahras.dz

Lien de revue

file:///C:/Users/DELL/Downloads/FEB_08_2022_Pp_07462-08257%20(1).pdf

Lien de l'article

file:///C:/Users/DELL/Desktop/Article%20SAYAH%20Sarra.pdf

file:///c:/users/dell/desktop/article sayah sarra.pdf

file:///C:/Users/DELL/Downloads/50FEB_22_00418.pdf