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PROTECTIVE EFFECT OF Calotropis procera OF TOXICITY OF MERCURIC CHLORIDE VIA ROUTE OF BIOCHEMISTRY PARAMETERS

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Mercury chloride is one of the most dangerous metals for health due to its volatility and its rapidity to pass through the human body. We undertook this study with the aim of investigating the detoxification of mercury chloride by the *Calotropis procera* plant taken from the Algerian Sahara. In this study, the toxicity of mercury chloride affected the kidney weights of male and female rats through increased weight. On the other hand, the plant *Calotropis procera* demonstrated a beneficial effect by restoring the weight of the kidneys. The results of this study demonstrated that the plant *Calotropis procera*. procera has a beneficial effect on the liver, which was able to restore its weight affected by the mercury chloride. Treatment of male and female rats with mercury chloride has also been found to lower blood urea levels, uric acid, proteins total, alkaline phosphatase and direct, indirect, total bilirubin levels. This toxicant caused an increase in blood sugar levels, blood creatinine, in male and female rats. No change in albumin levels was found in male and female rats. However, mercury chloride was found to increase cholesterol and triglyceride levels in male rats. The *Calotropis procera* plant restored cholesterol and triglycerides in male rats. This study can help to clarify that the detoxification of mercury chloride by *Calotropis procera* act directly on liver and kidney by ameliorating uric acid, blood sugar, creatinine, albumin, alkaline phosphatase, urea, total protein.

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1. INTRODUCTION

Mercury chloride is a toxic metal which can lead to the perturbation of the physiology of cells. For example, it increases the degree of urea [1] which stimulates the synthesis of the cellular immunity (cellularity). The same mechanism causes an increase in the blood urea level to induce the production of defense cells such as macrophages and neutrophils. This increases also the cellularity which the cancer uses as a matrix to proliferate. The perturbation of the biochemical parameters like the elevation of glycemia served like an advantage by mercuric chlorides to desequilibrate the power producer of cells. This mechanism of the blockage of the production of the insulin leads to the death of the cells [2]. Depletion of the production of the insulin hormone has been also observed in pancreatic cancer.

To detoxify the mercury chloride, more toxic plants similar to it can be used but in a beneficial way. Among these plants there is *Calotropis procera Calotropis procera* which is able to import new voices of detoxification of the mercury chloride. It is a plant known in the Algerian Tuareg population by "Torha". It protects from the toxicology of mercury chlorid by the regulation of biochemistry parameter that mercury chloride has desiquilibrated. Besides, it may decrease the toxicityof mercury chloride through biochemical pathways. It impeaches mercury chloride to use them to increase the cellularity [3]. The objective of this study is to find new natural ways to decrease the toxicity of mercury chloride.

2. METHODS AND MATERIALS

2.1 Animals

The study was carried out on adult male and female *Ratus ratus* Ratus ratus rats of the wistar strain, obtained from the Pasteur Institute in Algiers. The weight of the rats at the time of the experiment was 250 g / kg / bw. The animals were kept in standard food and water ad libitum. They were grouped together in large polyethylene cages (six rats per cage) in an air- conditioned animal facility at a temperature of $25 \pm 2^{\circ}$ C with constant humidity (50 %) on a light / dark cycle of 12hrs-: 12 hrs hrs: 12hrs.

The air-dried sample (200g) was percolated using ethanol 1,3L for a period of 10 days. The extract were drained and concentrated under pressure using

Rotavapor (R110 at 40°C). The ethanol extract was allowed to dry and its weight was recorded. This was labeled CP1. Ethanol extract (10g) was dissolved in 60% aqueous methanol Aq.MeOH (150 ml), and partitioned with petroleum ether (150 ml), chloroform (150 ml) Ethyl acetate (150) ml sequentially. All fractions obtained were collected marcs after extraction with ethanol was repercolated with 5M hydrochloric acid (500 ml) for the period of 3 days. Aqueous acid fraction obtained was basified with solution of sodium hydroxide and portioned with chloroform. The chloroform fraction was collected in a weighted beaker (After evaporating excess chloroform using Rotavapor).

2.2 Traitement of Rats

The male and female wistar strain rats were divided into 10 (ten) lots of 6 (six) rats, each in the following order: Lot 1(one): control, Lot 2(tow) : plant, Lot 3(three) : Plant + mercury, Lot 4 (four): Mercury, Lot 5 (five): Mercury + C. Procera extract. The rats were treated with a dose of 0.20 mg / kg intraperitoneally for 19 (nineteen) days. The plant extract (10 ml) was injected into the rats by gavage for 19 days. The determination of biochemical parameters was done according to the method: Urea: kinetic Urease, uric acid: uricase, total bilirubin: direct DCA, Direct Bilirubin: DCA, Creatinine: uncompensated kinetic Jaffe, Glycemic: GOD, Albumin: Bromocresol Green, PAL: IFCC, Triglyceride: Triglyceride oxidase, Cholesterol: Cholesterol oxidase.

2.3 Statistical Analysis

In the present study, the results were analyzed using the ANOVA statistics to compare the significance between the groups. The results of comparison between the groups are significant if P < 0.05. The tukey test were used for multi-comparison between groups.

3. RESULTS AND DISCUSSION

3.1 Effects of Mercury Chloride and the Plant *Calotropis Procera* on the Weight of Maleand Female Rats

It is found that the treatment of male and female rats with mercury chloride at a dose of 0.20 mg/kg bw affects the total body weight (Fig, 1.a, b).

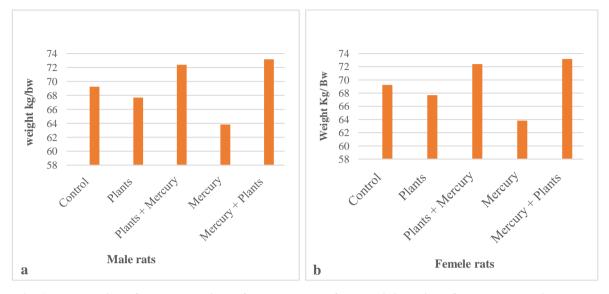
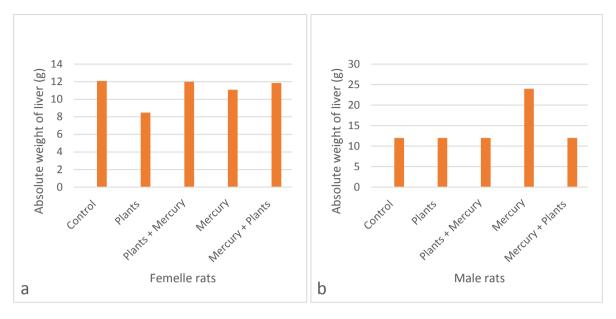


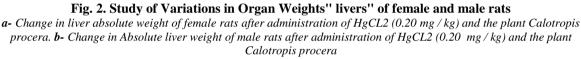
Fig. 1. a- Evolution of the body weight of the male rats after administration of mercury chloride, plant *Calotropis procera*, plant + mercury and mercury + plant at 0.20 mg kg for 20 days. b- Evolution of the body weight of the female rats after administration of mercury chloride, plant *Calotropis procera*, plant + mercury and mercury + plant at 0.20 mg kg for 20 days

Rats of both sexes showed signs of poor appetite and abstinence from food. The statistical analyzes by Anova one way and tukey test mutli-comparison demonstrated that there is a difference at p value <0,05between the body weight of male and female rats treated with the plant Calotropis procera and that of rats treated with mercury chloride. Rats treated with the plant *calotropis procera* showed lively behavior with a high appetite. This shows that C. procera positively influenced the weight of male and female rats and resulted in weight improvement. The plant Calotropis procera contain compounds like nitrogen, potassium, phosphorus, sodium, calcium, protein and carbohydrate [1] which can improve microflora proliferation and increase digestibility and weight. These mineral elements renew the energy of cells and stimulate appetite and weight gain. By these molecules the plant Calotropis Procera increased the weight in female and male rats and gave them more energy compared to the group of rats treated with mercury chloride. This shows that the Calotropis Procera plant can be considered an effective quality food and not a quantity food. The carbohydrates of the plant are different from the carbohydrates produced by mercury chloride which promote a toxic environment for the cells. However, calotropis carbohydrate will provide favorable conditions for cell development and activity. The carbohydrate molecules of the Calotropis procera protects against weight loss from mercury chloride and provides weight gain, energy and health. On the other hand, the toxicity by the chloride of mercury generated toxic carbohydrates which act negatively on the weight. An in vivo study on mice found that cardiac glycosides of the *Calotropis procera* like the usharin provided highly protective effects against loss of weight observed in diabetic rats administered by *Calotropis procera*. This shows that the *Calotropis procera* contains a molecular that reduce the toxicity of sugar in model of diabetics rat [4].

3.2 Effects of Mercury Chloride and *Calotropis procera* Plant on Liver Weight of Male and Female Rats

The results of this study demonstrated that mercury chloride increased the liver weight of male rats (Fig. 2). The increased liver weight of male rats is due to macrovascular and microvascular steatosis observed in histological studies of the effect of mercury chloride on male rats B [3]. Male rats restored the weight of liver. The same result was also seen in the histopathological study of liver tissue of groups treated by Calotropis procera, (mercury chloride + Calotropis procera) and (Calotropis procera + mercury chlorids) [3]. The Calotropis procera play an important role of the prevention against HgCl₂ increased liver weight in male rats. This action of Calotropis procera on weight of liver because it possesses strong antioxidant properties. The weight of liver of the female rats demonstrate that mercury chloride induced the decreased of weight of liver. On the other hand, the weight of the liver of female rats treated with Calotropis procera was restored. Calotropis procera have the potential hepatoprotective effect of on female rats and male rats.





3.3 Effects of Mercury Chloride and the Plant *Calotropis procera* on the Weight of Male and Female Kidneys

The administration of mercuric chloride with 0.20 mg / bw in the female and male rats induced significant increased the absolute and relative weight of kidney. In male rat groups, the weight of kidney is higher than those of females. Studies have demonstrated that the difference of the weight of kidney in both male and female rats is due to the expression of the organic anion transporters Oat. For example, in vivo studies in animal models of obesity in male rats have found that dysfunction of Oat 3 transporters leads to renal dysfunction [5]. Other studies on knockout rats have shown that oat1 capture more mercury chloride than oat 3 [6]. Studies on rats treated with mercury chloride found that low expression of Oat3 transporters in kidney basement membranes may be a defensive mechanism developed by the basal membrane cell to protect against mercury [7]. Besides, other studies found that the expression of renal transporters Oat3 is higher in the male rat than in the female [8]. This shows the protective role of Oat3 of the kidneys in the male sex. Oat 3s carry also AMP cyclic nucleotide molecules that are involved in functions of the male reproductive system. The increased kidney weights in male rats can also be attributed to cyclic AMP. The latter are expressed much more in the male rat than in the female. The regeneration of cyclic AMP nucleotides is of energetic "ATP" origin. The more sugar there is, the

more ATP there is and the less it is released, the more cyclic AMP nucleotides are generated and the greater the risk of cancer. The latter can cause diabetes [9]. Kidneys have been found in diabetic men to exhibit abnormal metabolism of cyclic AMP nucleotides. This metabolic imbalance appeared on the glomeruli by a change in diameter and weight. Field found in rats that the hormone glucagon stimulates an increase in the concentration of cyclic AMP [10]. The glucagon increases the level of this hormone in benign and much more malignant hyperplastic nodules. Other studies have found in hyperplastic liver cancer that the kidney enlarges too. According to the results of these studies there is a relationship between the organs of the human body, kidneys and sperm. This shows that when an organ is affected all organs are affected. The link between these organs is hormonal in origin. [11] found that the change in kidney weight is directly related to a hormone glucagon. The link of this hormone with the male genital system is the cause of kidney damage, and even some cases of cancer such as pancreatic cancer. This hormone, glucagon, has long been neglected compared to insulin but it is a molecule of life whose imbalance can lead to the loss of an organ chain, the liver, the kidneys, the pancreas and the sperm. This is also applied to mercury chloride known by its hyper glycemic effect. It generates a lot of ATP energy that it prevents it from being released. [3] found that following mercury chloride poisoning there is an accumulation of lipids in the liver in the form of

macrovascular steatosis in male rats. This shows that mercury chloride is capable of generating toxicity from glucose that it transforms into lipid and stores it in the liver. ATP not released by glucose can be transformed into the cyclic messenger AMP. In the case of intoxication by chloride of mercury, it produces in the organism a fever. The latter turns on the DNA of the spermatozoon and at the same time on the mercury attached to this DNA. The consequences of binding of mercury chloride to the DNA is its degradation into polynucleotide (unfragmented DNA). The latter acts badly on

sperm and spermatozoa which lose their viability. Sperm contaminated with mercury and unfragmented DNA will pass into the kidney and cause toxicity and contamination of kidneys; the result is blockage liquids. In the kidneys, sperm whose DNA is fragmented and whose energy and ATP has not been released into the oocyte are transformed into Cyclic Messenger AMP. The kidneys will act on the one hand by blocking the excretion tunnels and blocking a contaminated sperm with fragmented DNA by a state of hypertrophy and increased weight.

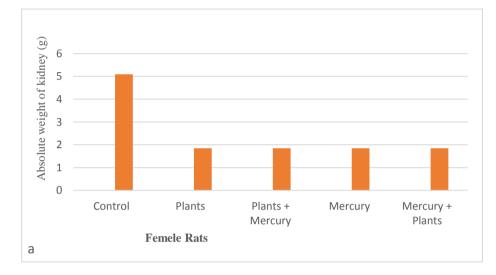
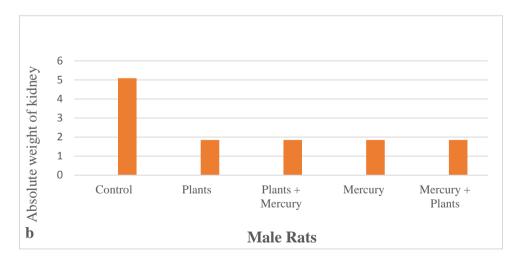
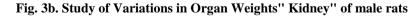


Fig. 3a. Study of Variations in Organ Weights" Kidney" of female

Change in kidney absolute weight of female rats after administration of HgCL2 (0.20 mg / kg) and the plant Calotropis procera





Change in Absolute kidneyweight of male rats after administration of HgCL2 (0.20 mg / kg) and the plant Calotropis procera

3.4 Effects of Mercury Chloride and the Plant *Calotropis procera* on the Biochemical Parameters of Female Rats Blood Urea Male and Female Rats

The treatment of male and female rats with mercury chloride causes a decrease in the blood urea level. In the female and males groups rats plasma urea levels has been restored by plant *Calotropis Procera*. This shows that the protective role of the *Calotropis procera* against the disturbances of the urea level caused by mercury in both sexes males and females. These results are in agreement with the study) [12] which also found that *Calotropis procera* protects the kidneys by maintaining normal blood urea levels. In addition, an investigation conducted by another study concluded that *Calotropis procera* contain acid like citric acid that can reduced the lethal effect of urea Kitagawa [3].

3.5 Uric Acid

According to our results, the administration of mercury chloride intraperitoneally at a rate of 0.20 mg / kg of body weight during a period of 20 days caused a highly significant decrease in uric acid in male and female rats. Studies have found that mercury chloride causes uric acid to convert to allantoin and through this action lowers uric acid levels [13,14] found that injecting rats with mercury chloride and uric acid inhibits the action of mercury chloride damaged the kidneys.

3.6 Blood Sugar of Male and Female Rats

Mercury chloride was found to increase blood sugar levels in male and female rats. The link between chloride and blood sugar is the pancreas. This small organ is the center of energy regulation. It is very sensitive to toxic attacks from mercury chloride. Studies in mice exposed to mercury chloride have shown that it causes damage to pancreatic cells [15]. Other studies have shown that heavy metals can directly attack the mitochondria of the pancreas and cause pancreatic cancer which imbalances blood sugar levels [3] found that mercury chloride induced accumulation of lipids in hepatocytes. In this, studies mercury chloride induced increased of glucose. This shows that mercuric chloride causes energy to rise and stores it in hepatocytes as fat. The plant C. Procera also increased blood sugar in the groups of rats treated with the plant, plant + mercury, mercury + plant. Our results showed that mercury increased blood sugar caused weight loss. While the plant Calotropis procera increased, blood sugar levels and resulted in increased weight in rats. This may be explained by the fact that the calotropis plant raised

blood sugar levels to give more energy to rats poisoned by mercury chloride. This shows that the plant does not have a hypoglycemic effect, which causes the release of the hormone glucagon. The movement of female and male rats observed after injection of C. This can be attributed to the presence of sweet components in this plant that can liberate energy. Studies by [16] carried out on this plant have found that this plant is rich in sweet components such as oxypregnan-oligoglycosides named calotroposides A and B. Other sugars of *calotropis procera* have also been disclosed in the plant Calotropis Procera: new oxypregnane oligoglycosides: calotroposides H – N (1–7) [17]. This study demonstrated that the components oxypregnaneoligoglycosides: calotroposides H - N (1–7) have anticancer activity against several types of cancer including prostate cancer and lung cancer. Calotropis procera can cope with cancer cells characterized by their high energy. It increased blood sugar levels without weight loss in female rats to give more energy to stop the extremely toxic and high-energy mercury chloride.

3.7 Creatinine

From male and female rats, our results have shown that mercury chloride causes an increase in blood creatinine levels in male and female rats. Studies have also found that mercury chloride causes an increase in blood creatinine levels and leads to kidney failure via disturbances in creatinine levels [18]. The results of our study showed that the plant *Calotropis procera* restored the creatinine level. This shows the role of calotropis in balancing one of the biochemical parameters most indicative of the proper functioning of the kidneys. This role is due to Calotropis procera's potential molecule uric acid which protects against the increase in creatinine by preventing the toxicity of Hg Cl2 [19]. The plant has an action on creatinine and effect protector on the kidney. Chemical studies on the plant Calotropis procera have revealed several components including cardinolides. Recent studies have shown that these components are cardioids which play a protective role against autosomal dominant polycystic kidney disease (ADPKD) [20].

3.8 Serum Proteins

Treatment of female rats with mercury chloride at a dose of 0.20 mg kg / bw caused a drop in serum protein levels. Treatment of female rats with the plant *Calotropis procera* corrected the decrease in serum protein levels. Studies carried out on Calotropis have revealed the plant's richness in proteins such as proteases, dismutases, peroxidases, chitinases and proteases containing cysteine and acid proteases [21].

This explains its nutritional role against mercury chloride by maintaining and preservation of serum proteins. The plant corrected the decrease in serum protein levels.

3.9 Cholesterol

The results showed that there was no difference in cholesterol levels between the groups of female rats. Our results demonstrated no effect of mercury chloride and the plant on cholesterol levels in female rats. This may be due to the physiology of female rats and their possessing factors that protect them against cholesterol disturbances. However, mercury chloride was found to increase cholesterol levels in male rats. The Calotropis procera plant restored cholesterol levels in male rats. Chemical studies have revealed the presence in calotropis of acidic molecules such as furilic acid which protect against myocardial infarction and restore cholesterol levels in the blood of rats exposed to mercury chloride [22]. There is also another study which showed the role of the plant *Calotropis procera* in lowering cholesterol in diabetic rats. These shows that this plant has a significant cholesterol lowering effect; and that by this effects it protects rats against mercury chloride which unbalances cholesterol levels. By this detoxifying action of Calotropis procera decreased the toxicity of mercury chloride and protected the organs from the consequences and deleterious effects of mercury.

3.10 Albumin Male and Female Rats

Analyzes of biochemical parameters such as albumin showed that there was no difference between the groups of female rats. The same result was observed in males rats, there is no difference between groups and absence of effect of plants on rats.

3.11 Male and Female Rat Triglycerides

Our results demonstrated the plant's lack of effect on triglyceride levels in female rats. The result of analysis of triglycerides in male rat demonstrate that mercury chloride increased TG. The group male rat received the extract of *Calotropis procera* significantly decreased TG content when compared with the mercury group male rat. The result of the study conducted by [23] report that *Calotropis procera* reduced the TG significantly analyzed also the anti-hypeglyceride beneficial effects of *Calotropis procera* on diabetic rat.

3.12 Alkaline Phosphatase Male and Female Rats

Our results have shown that mercury chloride causes a highly significant decrease in the level of alkaline

phosphatase in female and male rats. This shows that mercury chloride caused a deficiency in the level of the alkaline phosphatase enzyme. This deficiency of this enzyme can be explained by a dephosphorylation of the hepatic phosphorus receptors. Our results also demonstrated that the plant Calotropis procera restored the level of alkaline phosphatase in male and female rats treated with the plant+mercury, mercury+plant and plant compared to that of mercury chloride. This shows that the plant corrected the deficiency of alkaline phosphatase caused by mercury chloride. The return to normality of the level of alkaline phosphatase shows that the plant has an effect on the activity of this enzyme. Studies have shown that the leaves, flower and root of the Calotropis procera plant are rich in the enzyme alkaline phosphatase [24]. Other studies have also shown that the plant has a protective action on the kidneys via the alkaline phosphatase [25] found that patients with renal failure associated with sepsis treated with alkaline phosphatase protect their kidneys against systemic inflammation and decrease markers of renal tubule damage. Other studies have found that alkaline phosphatase plays an important role in inhibiting acute kidney injury AKI in an animal model of childhood circulatory cardioplmonary disease [23].

3.13 Total Bilirubin Male and Female Rats

Our results showed that the plant corrected the level of total bilirubin.

3.14 Direct, Indirect and Total Bilirubin in Male and Female Rats

Our results demonstrated that there was no change in the level of direct, indirect and total bilirubin in female rats. This can be explained by the genetic susceptibility of the female sex which is resistant to toxins like mercury chloride via bilirubin. The female is known for her production of low levels of the hormone testosterone. The latter is beneficial for both the female and the male sex. The results show that the level of bilirubin is low in male rats treated with mercury chloride. Studies have found that variations in bilirubin between male and female sex is linked to hormones [26]. Disturbances in the hormone testosterone influence changes in bilirubin levels in males. The latter produces more testosterone hormone than the female. Studies have found that increased testosterone levels in humans are the cause of liver cancer [27]. The liver toxicity seen in mercury chloride poisoning is related at high testosterone and low bilirubin levels. This shows that mercury chloride works through a mechanism that connects two vital organs, the reproductive system and the liver. This mechanism generated by mercury chloride imbalances the hormone testosterone on the one hand and bilirubin on the other. Another research has found that the difference in bilirubin changes is due to the enzyme bilirubin uridine diphosphateglucuronosyltransferase. Male and female rats exert opposite effects of the enzyme uridine diphosphateglucuronosyl-transferase. The latter is higher in females than in humans in the liver [28]. According to the results of in vivo studies carried out on extracts of the *calotropis procera* to analyze these effects visà-vis hepatitis induced by the paracetamole; they have found that it restores blood bilirubin levels [29]. This shows that Calotropis procera have the potential hepatoprotective effect via equilibrate the biochemical levels of bilirubin. Other studies have found that changes in bilirubin have a maternal origin related to milk. Babies who breastfeed breast milk have been found to have elevated bilirubin levels compared to babies who breastfeed artificially [30]. This shows that maternal milk has a nutritional action via the enzyme B-glucuronidase which increases bilirubin. It has also been found in the milk of babies who naturally breastfeed the molecules pregnane-3a, 20 B- diol, interleukin IL1B,Bglucuronidase,epidermal growth factor, and alphafetoprotein. The presence of the pregnane 3a 20 Bdiol is thought to inhibit bilirubin's conjugation which in turn impede bilirubin excretion.

3.15 Effects of Mercury Chloride and the Plant *Calotropis procera* on the BiochemicalParameters of Male Rats

3.15.1 Cholesterol

Mercury chloride was found to increase cholesterol levels in male rats. The *Calotropis procera* plant restored cholesterol levels in male rats. Chemical studies have revealed the presence in calotropis of acidic molecules such as furilic acid [31]. Studies have found ferulic acid protects against myocardial infarction and restores blood cholesterol levels in rats exposed to mercury [12].

3.15.2 Urea

The results showed that treatment of male rats with mercury chloride resulted in an increase in urea levels. Treatment of male rats with plant + mercury and mercury + plant restored urea levels. This shows the role the plant *Calotropis procera* plays in restoring urea levels and decreasing toxicity. *Calotropis procera* protects the kidneys by maintaining the urea level at normal.

3.15.3 Albumin

The results of this study showed that mercury chloride caused a decrease in albumin levels in male rats. A decrease in albumin, globulin ratio related to a decrease in total cholesterol levels was reported by Meltem Uzunhisarcikli, [32].

3.15.4 Bilirubin Total, Direct, Indirect

According to the results of our study, mercury chloride caused a drop in the level of total bilirubin, direct, indirect compared to the control group. Histological studies of male rat treated with mercury chloride demonstrate the appearance of macrovacuolar and somewhat micro-vacuolar, diffuse steatosis [3]. In this study we found in bad rats an increase in blood sugar. The latter acts directly on the liver. The high blood sugar levels may be the cause of nonalcoholic steatosis in people with diabetes. This shows that blood sugar can target the liver and cause an imbalance in bilirubin levels. Bilirubin is sensitive to the action of mercury chloride in male rats compared to female rats. This shows that male rats are less resistant to the action of mercury chloride than female rats. The degradation of bilirubin appears in male rats more than female rats. This in relation to hemoglobin of the male sex is different from female rats. Male sex needs more iron and energy release from hemoglobin. In the case of mercury chloride poisoning, there will be no renewal of red blood cells. This generates toxic hemoglobin. This phenomenon triggers the movement of neutrophils to attack this hemoglobin. When neutrophils swallow this hemoglobin, they become the trigger and amplifier of inflammatory reactions.

Another factor is the sperm, although the latter are physiologically present in the female male fertility problem. This function is protected to ensure the continuity of the human being.

Recently studies have revealed that there are macrophages which function as guardians of sperm all by preventing their breakdown. However, in circumstances of toxicity by mercury chloride the role of these cells is blocked and the sperm are no longer protected. At this point comes other types of cells, the white neutrophil cells, which act directly on the sperm. By swallowing the sperm, it swallows the lipids contained in them. This increases the level of lipids in the neutrophils and then becomes toxic and an agent of inflammation instead of its normal defense function [33]. When sperm are broken down, they become foreign to the body which causes the production of anti-sperm antibodies, which directly attack the hemoglobin and cause bilirubin imbalance

in the disease. In the case of women, due to the absence of sperm, they are more protected than men and their bilirubin is balanced compared to men.

4. CONCLUSIONS

The toxicity of mercury chloride is a health problem for the dangerous metal it contains. In the body, this metal circulates in the blood and can unbalance several organs by disrupting biochemical parameters. A chain of connection between these biochemical parameters is at the origin of serious damage to the kidneys and liver. The return to medicinal plants has released the detoxification pathways of mercury chloride through the biochemical parameters bay. In this study, we shed light on a plant from the Sahara of Algeria, Calotropis procera, known by the Tuaregs for its beneficial actions for the body. Contrary to preconceived ideas, on the toxic properties of the plant. Conversely, this work has been investigated on this plant and secrets have been revealed prove that Calotropis procera still has a bright future in the detoxification of mercury chloride. In this study, it is found that the calotropis will restore the weight of the rats and act on the appetite; it gives energy and the movement by the berry of the glycaemia; and it gives the body to proteins to face the losses of the blood sugar and weight. It also worked on urea to protect the kidneys and pancreas. It also worked on bilirubin to disturb the action of mercury chloride on the liver. Calotropis procera made the action of mercury chloride less toxic by its actions to balance biochemical parameters. Our study unveiled a new mechanism for detoxifying a metal as strong and toxic as mercury chloride. This study brings a new understanding in the detoxification of mercury chloride using the plant Calotropis procera. The results of this study demonstrated that the Calotropis procera acts indirectly on mercury chloride by bay biochemical parameters. His plant balances the parameters disturbed by mercury chloride.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kabore A, Kondombo CP, Gnanda BI, Kologo I, Konate A, Yougbare B, Traore A, Tamboura

H, Belem AM. Supplementation Effects of *Calotropis Procera* Dried Leaves on the Growth Performance of Sheep in Dry Season in Burkina Faso. J. Dairy Veterinary & Animal Research. 2017;6:247-250. DOI: 10.15406/jdvar.2017.06.00169

 Belfarhi L, Chouba I, Amri N, Boukris N, Tahraoui A. Histological and hormonal study of the protective effect of the *Calotropis procera* against the toxicity of mercury chloride. Natural Systems and Resources. 2020;10:5-14. DOI:https://doi.org/10.15688/nsr.jvolsu.2020.2

.1

 Murugan V, Ganesan J, Erusan B. Ameliorative potential of ferulic acid on cardiotoxicity induced by mercuric chloride. Biomedicine and Preventive Nutrition. 2014; 4:239-243.

DOI: 10.1016/j.bionut.2014.02.005

- Dwivedi A, Chaturvedi M, Gupta A, Argal A. Medicinal utility of *Calotropis procera* (Ait.) R. Br. as used by natives of village Sanwer of Indore District, Madhya Pradesh, International Journal of Pharmacy and Life Science. 2010;3:188-190.
- 5. Rathod NR, Raghuveer I, Chitme HR, Chandra R. Free Radical Scavenging Activity of *Calotropis gigantea* on Streptozotocin-Induced Diabetic Rats. Indian journal Pharmascetical Science. 2009;71:615–621. DOI: 10.4103/0250-474X.59542
- Gisela Di Giusto, Naohiko Anzai, María L. Ruiz, Hitoshi Endou, Adriana M. Torres. Expression and function of Oat1 and Oat3 in rat kidney exposed to mercuric chloride. Arch Toxicol. 2009;83(10):887. DOI: 10.1007/s00204-009-0445-8.

Ljubojevic M, Herak-Kramberger, Hagos Y,

Bahn A, Endou H, Burckhardt G, Sabolic I. Rat renal cortical OAT1 and OAT3 exhibit gender differences determined by both androgen stimulation and estrogen inhibition. Am J Physiol Renal Physiol. 2004;287:124– 138.

DOI: 10.1152/ajprenal.00029.2004.

 HaiBo Y, Zhao FX, Wei L, Yu D, Bin X. The Protective Role of Procyanidins and Lycopene against Mercuric Chloride Renal Damage in Rats. Biomedical and Environmental Sciences. 2011;24(5):550-559.

DOI: 10.3967/0895-3988.2011.05.015

 Reuben C, Sheldon M, Epstein, James BF. Glucagon and Prostaglandin E1 Stimulation of Cyclic Adenosine 3', 5'-Monophosphate Levels and Adenylate Cyclase Activity in Benign Hyperplastic Nodules and Malignant Hepatomas of Ethionine-treated Rats. Cancer Research. 1973; 33:1970-1974.

- Cortes P, Dumler F, Venkatachalam K, Goldman J, Sastry KS, Venkatachalam H, Bernstein J, Levin NW. Alterations in glomerular RNA in diabetic rats: Roles of glucagon and insulin. Kidney International. 1981;20:491-499. DOI: 10.1038/ki.1981.166
- 11. Abid A, Tabassum M. Protective efficacy of *Calotropis procera* leaf hexane extract against ibuprofen induced kidney toxicity in albino rats. Annals of Jinnah Sindh Medical University. 2018;4:13- 22.
- 12. Kitagawa I, Zhang R, Park J.D, Baek N.I, Takeda Y, Yoshikawa M, Shibuya H. Indonesian medicinal plants. I. Chemical structures of calotroposides A and B, two new oxypregnane- oligoglycosides from the root of Calotropis gigantea (Asclepiadaceae). Chem. Pharm. Bull. 1992;40:2007. DOI: 10.1248/cpb.40.2007.
- Sabrin RM, Gamal AM, Mohamed Zayed F, Samir AR. Hydroxyirilone 5-methyl ether and 8-hydroxyirilone, new antioxidant and αamylase inhibitors isoflavonoids from Iris germanica rhizomes. Bioorg Chem. 2018; 70:192-198. DOI: 10.1016/j.bioorg.2016.12.010. Epub 2016 Dec 30.
- Romero F, Pérez M, Chavez M, Parra G, and Durante P. Effect of uric acid on gentamicininduced nephrotoxicity in rat- role of matrix metalloproteinase 2 and 9. Basic and Clinical pharmacology and toxicology. 2009;105(6): 416-424.

DOI: 10.1111/j.1742-7843.2009.00466.x

15. Kuo-Liang C, Shing-Hwa L, Chin-Chuan Su, Cheng-Chieh Y, Ching-Yao, Yang. Kuan-I L, Feng- Cheng Tang, Ya-Wen C, Tien-Hui L, Yi-Chang S, Chun-Fa H. Mercuric Compounds Induce Pancreatic Islets Dysfunction and Apoptosis *in vivo*, International Journal of Molecular Sciences. 2012;13(10):12349– 12366.

DOI: 10.3390/ijms131012349.

16. Kitagawa I, Zhang R, Park JD, Baek NI, Takeda Y, Yoshikawa M, Shibuya H. Indonesian medicinal plants. I. Chemical structures of calotroposides A and B, two new oxypregnane- oligoglycosides from the root of *Calotropis gigantea* (Asclepiadaceae). Chemical and Pharmaceutical Bulletin. 1992; 40:2007-2013.

DOI: 10.1248/cpb.40.2007.

17. Paller MS. Free radical scavengers in mercuric chloride-induced acute renal failure in the rat.

Journal Laboratory Clinic Medicine. 1985; 105:459-63.

 Areej MA, Shagufta P, Ghada AF, Attiq R, Afsar K,Rashad M, Laila MF. Evaluation of antiulcer and cytotoxic potential of the leaf, flower, and fruit extracts of *Calotropis procera* and isolation of a new lignan glycoside. Evidence-based Complementary and Alternative Medicine; 2017. Article ID 8086791. Available:https://doi.org/10.1155/2017/808679

Available:https://doi.org/10.1155/2017/808679 1.

 Cleverson Diniz TF, Jefferson SO, Maria RAM, Nívea Maria RM, Maurício PS, Laurival A Villas-Boas, Márcio VR. Enzymatic activities and protein profile of latex from *Calotropis procera*. Plant Physiol Biochem. Plant Physiol Biochem. 2007;45(10-11): 781-9.

DOI: 10.1016/j.plaphy.2007.07.020.

- 20. Stéphanie C. Effet des composés phénoliques sur le vieillissement cardiaque et rénal: Etude expérimentale chez le rat Soutenue le 6 juillet 2018 devant la Commission d'Examen. Thèse de Doctorat; 2018.
- 21. Bhaskar VH, Patel MP. Evaluation of antihyperglycemic activity of extracts of *Calotropis procera* (Ait.) R.Br on streptozotocin induced diabetic rats. Global Journal of Pharmacology. 2009;3:95-98.
- Malik CP, Mehan M, Vermani S. Distribution of Alkaline Phosphatase in Pollen By Grains and Pollen Tubes of *Calotropis procera*. Biochemie und Physiologie der Pflanzen. 1975;167:601-603. Available:doi.org/10.1016/S0015-3796(17)31317-3
- 23. Eric MW, Linda LW, Brenda YH, Jun-Fang J, Wei J, Sandi AK, Sumodh K. Gender differences in hepatocellular cancer: disparities in nonalcoholic fatty liver disease/ steatohepatitis and liver transplantation. Hepatoma Research. 2018;4:2-17.
- 24. Femke HO, Pleun H, Peter P. Innovative Drugs to Target Renal Inflammation in Sepsis: Alkaline Phosphatase. Frontiers in Pharmacology. 2019;23:1-9.
- Yoshihiro M, Yoriko M, Hiroshi F, Sayuri N, Takahide Y, Katsuyuki M, Asami M, Hiroshi S, Robert HT, Yoshihiro, Takeuchi. Bilirubin uridine diphosphate-glucuronosyltransferase variation is a genetic basis of breast milk jaundice. J Pediatr. 2014;165:36-41. DOI: 10.1016/j.jpeds.2014.01.060.
- 26. Maurizio Muraca, Johan Fevery. Influence of sex and sex steroids on bilirubin uridine diphosphate-glucuronosyltransferase activity

of rat liver. Gastroenterology. 1984;87:308-313.

- 27. Ramachandra S, Setty, Absar AQ, Viswanath HM, Tushar P, Prakash T, Prabhu K, A Veeran Gouda. Hepatoprotective activity of *Calotropis procera* flowers against paracetamol-induced hepatic injury in rats. Fitoterapia. 2007;78:451-4.
- Lewi S, Walter P, Clarke TK. Allaitement maternel et hyperbilirubinémie du nouveau-né BiolNeonate. 1964;7:294–304.
- 29. Michelle M. White, Patrick Geraghty, Elaine Hayes, Stephen Cox, William Leitch, Bader Alfawaz, Gillian M. Lavelle, Oliver J. McElvaney, Ryan Flannery, Joanne Keenan, Paula Meleady, Michael Henry, Martin Clynes, Cedric Gunaratnam, Noel G. McElvaney, and Emer P. Reeves. Neutrophil Membrane Cholesterol Content is a Key Factor in Cystic Fibrosis Lung Disease. E BioMedicine. 2017; 23:173-184.

DOI: 10.1016/j.ebiom.2017.08.013.

- Gartner LM, Herschel M. Jaundice and breastfeeding. Pediatric Clinics. 2001;48(2): 389-400.
- 31. Song K, Zhu X, Zhu W, Li X. Preparation and characterization of cellulose nanocrystal extracted from *Calotropis procera* biomass. Bioresources and Bioprocessing. 2019;6(1): 1-8.
- Kalender S, Ogutcu A, Uzunhisarcikli M, Açikgoz F, Durak D, Ulusoy Y, Kalender Y. Diazinon-induced hepatotoxicity and protective effect of vitamin E on some biochemical indices and ultrastructural changes. Toxicology. 2005;211(3):197-206.
- 33. Swain SD, Rohn TT, Quinn MT. Neutrophil priming in host defense: role of oxidants as priming agents. Antioxidants and Redox Signaling. 2002;4(1):69-83.

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