Prophylactic Effect of A Probiotic Strain *Lactobacillus Rhamnosus* Against Aluminum Chloride-Induced Intoxication in Wistar Rats: Neurobehavioral and Hematobiochemical Studies

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Abstract

Purpose: Aluminum (Al) and its various forms are environmental xenobiotics that pose great threats to public health. The probiotic strain has been reported to have important protective effects against aluminum cytotoxicity. Therefore, the current study was designed to assess the disruption of neurobehavioral and hematobiochemical parameters caused by chronic exposure to AlCl3, and then explore the protective effects of the probiotic strain *Lactobacillus rhamnosus* against these adverse in male rats.

Method: Thirty-two animals were gathered into four groups: The first group served as control. The second group received 100mg AlCl3/kg bw for 12 weeks. However, the third group was administered 10mL probiotic strain /Kg (108 CFU/ml) bw/d daily for 4 weeks. Finally, group 4 received AlCl3 for 12 weeks, then the treatment was continued with probiotic for 4 weeks.

Results: AlCl3 produced a decrease in body and brain weights with respect to their control. The results obtained also showed significant depression and anxiety-like behavior in the intoxicated animals, with a disturbance of the tested hematobiochemical parameters, particularly in renal and hepatic biomarkers. Overall, probiotics prevented enduring AlCl3-induced depression-like behavior in intoxicated rats. The results of the hematobiochemical, renal and hepatic analyses show a correction of the values after the administration of probiotics compared to those of intoxicated and untreated animals.

Conclusion: The probiotic lactobacilli would be an alternative to reduce AlCl3 toxicity.

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Introduction

Aluminum (Al) is the most naturally occurring metal on the earth's surface and is a trivalent cation found in its ionic form (Al3+) in most animal and plant tissues and in natural waters. Diverse aluminum compounds are produced and used in several fields such as water treatment, food additive manufacturing, dyes, pharmaceuticals, in the manufacture of kitchen utensils and food packaging (Berihu et al., 2015). Daily, moderate levels of this metal enter the body and can accumulate in certain organs. Most of Al ingestion is provided by food in different ways and water provides the highest biological availability to be absorbed by the gut (Karbouj, 2009; Douichene, 2016). No beneficial biological role has been attributed to aluminum; long considered harmless, aluminum is now considered a toxic metal, including a neurotoxicant (Gupta et al., 2005). In recent years, an increase in the number of diagnoses of neurodegenerative diseases (such as Alzheimer's disease) has led more and more scientists to investigate the etiology of these diseases. Some of them have found a direct link between these diseases and the presence of high aluminum concentration in the tissues of affected patients (Sanchez-Iglesias et al., 2007). Al enters the brain and crosses the blood-brain barrier (BBB) via specific high-affinity transferrin receptors that are expressed in the BBB (Thenmozhi et al., 2015). Transferrin receptors also exist in the cerebral cortex, hippocampus, septal nuclei, and amygdala where Al can be accumulated (Xiao et al., 2011).

On the other hand, natural resources are full of beneficial virtues for humans, in addition to their diet (Ramdane, 2008). Several studies have been undertaken to evaluate the impact on health of certain non-nutritional food components such as micronutrients, prebiotics, and probiotics (Aitbelgnaoui, 2006). Currently, probiotic strains are often incorporated into marketing strategies to build health claims in response to consumer attention for a "healthy" lifestyle (Bahri, 2016). Probiotics are dietary supplements consisting of live microorganisms that favorably influence the host animal by improving the balance of its gut flora (Rivièr, 2020). Most of them are lactic acid bacteria ingested by consumers via fermented dairy products. The most used are *Lactobacillus and Bifidobacterium* (Wanchai et al, 2018). *Lactobacilli* are representative of the beneficial human gut microbiota and therefore are the most prominent microorganisms as probiotics (Kesarcodi et al., 2008). Moreover, the evaluation of the effects exerted by probiotics through in vitro and in vivo studies could constitute a more rational approach in the selection of these microbial agents to prejudge their therapeutic potentialities (Aitbelgnaoui, 2006).

In the light of these data, our research work consists, on one hand, in estimating the incidence of Aluminium chloride ($AlCl_3$) intoxication in wistar rats and, on the other hand, in evaluating the therapeutic effect of probiotics against $AlCl_3$ toxicity by exploring different functions such as neurological, hepatic, renal and hematological function.

Materials and methods

Preparation of milk fermented with the probiotic strain

Lactobacillus rhamnosus is obtained as a Swab containing a pellet of freeze-dried microorganisms (ATCC 53103- KWIK STIK X2, Alliance bio-expertise). The strain is grown in De Man, Rogosa, and Sharpe (MRS) broth at 37°C. After 24 hours of incubation, a subculture was performed on MRS agar and incubated at 37°C for 48 hours. Two colonies were then transferred to 9ml of semi-skimmed milk and incubated at 30°C for18h. From a standard inoculum, 200ml of sterile semi-skimmed milk is inoculated with 1ml of *Lactobacillus rhamnosus* (i.e., 10^8 CFU/ml) (Benreguieg et al., 2013; Mahmoudi, 2014), the cultures are incubated, and the resulting coagulate is then stored at 4°C until it is presented to the animals.

Origin of the animals and housing conditions

We used twenty-four healthy Albino rats of the Wistar strain were obtained from the local animal house of the department of biology.

The number of suffering animals was minimized following the guidelines of the European Council Directive (86/609/EEC).

The animals were acclimatized at the animal house in professional plastic cages (43 x 28 x 5 cm). Then, were randomly divided into 4 groups of 8 animals in each (Fig. 1). The room they occupy is maintained at a temperature of (22 to 23 C°) and is subjected to a constant light cycle (alternating 12/12 hours darkness/light). The animals have access to water bottles and feeders. The assessment of body weight and brain weight of all tested rats were recorded weekly throughout the exposure period within the groups.

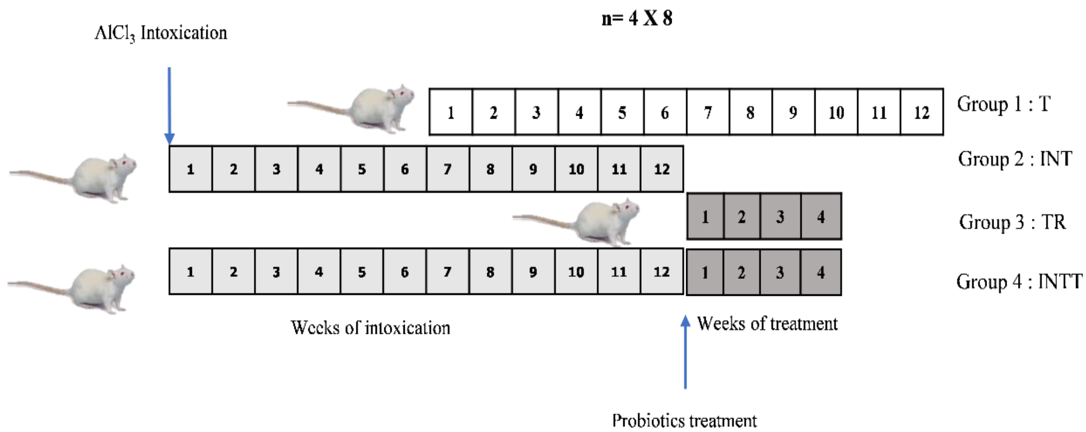

Figure 1. Experimental protocols used in this work. (Group 1: T): animals have not undergone any treatment. (Group 2: INT): Animals were intoxicated by oral administration of aluminum chloride ($AlCl_3$) at 100 mg/kg bw/d for 12 weeks (El-Nahrery, 2015). (Group 3: TR): animals were fed with probiotic strain (Prob) by oral administration at 10^8 CFU/ml,10ml/Kg bw/d; for 4 weeks (Nimgampall and Kuna, 2017; Woo et al., 2014). (Group 4: INTT): Animals were intoxicated by oral administration of aluminum chloride ($AlCl_3$) at 100 mg/kg bw/d for 12 weeks, then were fed with probiotic strain (Prob) by oral administration at 10^8 CFU/ml,10ml/Kg bw/d; for 4 weeks.

Neurobehavioral study

During the exposure period several neurobehavioral parameters were assessed including locomotor activity, motor coordination, anxiety level, depression and short-term and spatial memory, using various devices (Open Field, Dark and Light, Forced Swimming Test, Y maze test and Morris pool) respectively.

Open Field Test

The Open Field (OF) test was originally described and developed by Hall (1938) and is regularly used in many studies as a test of locomotor and exploratory activity and as a predictor of emotional reactivity in rodents, which are considered to prefer confined, enclosed, dimly lit spaces and tend to avoid this stressful environment. In this study, the mouse was placed in an open field (e.g., lit with a dark background scattered with lines delineating tiles (10 x 10 cm)) where the mouse was initially placed in one of the four corners of the open field with its head facing the corner (Dauge et al., 1989).

Dark and Light Test

According to Crawley and Goodwin, (1980); Misslin et al, (1989) this test is commonly used in behavioral studies where it is based on the aversive properties of the rodent towards light in order to assess its anxiety state. The device consists of a box with two equal compartments (L = 22 cm; W = 16 cm; H = 23 cm) separated by a small opening 6 cm high and 5 cm wide, one of which is black, and the other is brightly lit. Each subject was placed in the corner of the wall opposite the central opening at the level of the dark compartment and allowed to explore this new environment for 3 minutes. The parameters measured after the three minutes of exploration are the time spent in both compartments during the 5 minutes of experimentation, which allows us to compare the exploratory activities of these animals in both chambers by determining their anxiety levels.

Forced Swimming Test

This test assesses the state of resignation, which is a depressive behavior in rodents, and results in significant immobility according to its first founder (Porsolt, 1977). The experimental device is a transparent Plexiglas cylinder 20.7 cm in diameter and 39 cm high filled 3/4 with water at a temperature of 22±1°C in which the mice are successively subjected to this forced swimming test for 3 minutes, the parameters to be measured are: The mobility time when the animal is actively swimming with all four legs. The immobility time during which the animal only floats (low amplitude movements) which reflects behavioral desperation.

Three-armed maze (Y maze test)

This test can be widely applied to study short-term memory in older rodent models. Experiments with the Y maze have been conducted to assess the willingness of rodents to explore a new environment and spontaneous switching in animals. The test consists of three Y-shaped arms with a black color. The animal was placed in the middle of the maze and the rat was allowed to make decisions about the direction of travel between the three arms. The experiment was considered correct if the rat visited all three arms consecutively, while visiting an individual arm more than once in three alternations was considered wrong (Prieur and Jadavji, 2019).

% alternations = (total number of alternations/ number of arms entered) x 100.

The Morris pools

Learning ability, spatial orientation and spatial memory in rodents were assessed using the Morris pool test (Morris, 1984). The experimental set-up is a circular pool (diameter 160 cm; height 60 cm) filled with water at a height of 30 cm and maintained at a temperature of 22°C ±1. The platform (10 cm in diameter and 28 cm high) is covered with a grid to facilitate the grasping of the animals. A non-toxic white paint is dissolved in the water to make it opaque. The tank is installed in an experimental room with various visual cues on the walls. The experimenter is hidden from the animal's view and its movements are tracked by a video camera. The pool is virtually divided into quadrants: North-East (NE), South-East (SE), North-West (NW), South-West (SW) and the acquisition phase lasts 4 days with 4 trials per day separated by 40 min. The tests are carried out between 9am and 12pm. The platform is placed in the NW quadrant 2 cm below the water surface. The rat was placed in the tank with its head against the wall at one of the four cardinal points. The time taken by the animal to reach the platform is recorded. Each trial lasts 60 seconds. If the rat cannot find the platform at the end of the trial, it is placed on it by the experimenter for 20 sec. The probe test is performed the day after the last day of training. The platform is removed from the pool and the animal is placed in the South (S). The time spent in the quadrant where the platform was located during the acquisition phase (NO) is measured in a single 60-second trial. After 2 hours of the probe test, the visible platform phase takes place. The platform is placed in the middle of the NW quadrant and made visible with a black flag. 4 trials of 60 seconds each, separated by 40 minutes, are conducted by placing the rat successively at the 4 cardinal points. The time taken to reach the platform was measured.

Hematological Assay

Blood taken with EDTA was used for the determination of total red blood cells (RBCs), white blood cell (WBC) count, hematocrit percentage (HTC), hemoglobin (Hb) and platelet count (PLT) using an automatic cell counter (Mindray BC 3000 plus).

Biochemical assay

Determination of the kidney and liver parameters

All animals were killed at the same time. Blood samples were taken from all rats in heparinized tubes and then centrifuged. In the present study, we chose plasmatic biochemical parameters related to liver and kidney function. We determined the glucose content, uric acid, creatinine, cholesterol and triglycerides and levels of enzymes such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT). These enzymes were examined by routine colorimetric methods using commercial kits (Kaplan and Murray,1984; Thomas,1992)

Expression and statistical analysis of results

The results are expressed as the mean (M) of the individual values plus the standard error of the mean (S.E.M). The comparison of two means is performed by a student's t-test. The comparison of several means is performed by an analysis of variance (ANOVA) with the intoxication factor (AlCl3, T) and/or the treatment factor (Prob, AlCl3), possibly followed by the student-Newman-Keuls post-hoc test. Statistical analyses were performed with Sigma Stat software.

Results and discussion

This work focuses on the study of the impact of a probiotic treatment and a chronic intoxication with aluminum chloride on disorders that can generate to the different organs of Wistar rats.

Assessment of the weight parameters

The results of body weight show that $AlCl_3$ intoxicated animals represent a significant ($p<0.001$) decrease in weight to that of control animals during the 12 weeks of experimentation. This indicates that $AlCl_3$ causes a decrease in pity (Thenmozhi et al., 2015). This reduction is probably due to the anorexigenic effect of $AlCl_3$, as Al acts on the decrease of the synthesis pathways of serotonin and dopamine levels, these two neurotransmitters are directly involved in the regulation of digestive, feeding behavior and satiety control (Boutaleb et al., 2017). On the other hand, we note a weight gain for the rats of the treated batch after the administration of the probiotic, these results agree with those of Idoui et al (2008). However, the results of brain weight show that there is a significant decrease ($p<0.001$) in AlCl3 intoxicated rats compared to control rats which may be due to the toxic effect of Al during their accumulation in these organs. These results agree with those of Abdulmalek et al (2015) and Ajibade et al (2011) on the other hand there is an increase in organ weights after administration of the strain in both intoxicated and treated rats which suggests that the administration of the probiotic reflects a better development of internal organs according to Coudeyras and Forestier

(2010), (Table 01).

Table 1. Evaluation of weight parameters of control, AlCl3, and Prob treated rats

Lots	Body weight (g)	Brain weight (g)
T	335,75 ± 1,29	2,19 ± 0,02
INT	275,38 ± 1,75***	1,79 ± 0,01***
TR	333,7 ± 4,7	2,17 ± 0,01
INTT	298,35 ± 2,95***	2,01 ± 0,02***

Values are expressed as mean ± SEM (***: $p<0.001$).

These results suggest that Al toxicity causes a decrease in the number of glial cells, and a reduction in the number of neurons in specific regions in the hippocampus and cerebral cortex. Al stimulates programmed death (apoptosis) of neurons in the hippocampus and cortex primarily through down-regulation of anti-apoptotic factors and up-regulation of pro-apoptotic factors (Prema et al., 2016). Al is characterized by a strong positive charge that facilitates its binding to some atoms of the amino acids of various proteins. Indeed, Al can form a complex with proteins by inducing conformational changes that can inhibit their degradation, thereby enhancing their production and aggregation in tissues. Prolonged exposure to Al can cause several disturbances in the body such as altered functions, vital reactions such as membrane disruption, loss of calcium homeostasis, disruption of mitochondrial respiration as well as Al causes neurotoxicity by their accumulation in the brain and finally the death of neurons (Wang et al., 2016). Thus, this exposure to aluminum could influence food intake, gastrointestinal tract, and intestinal food absorption in rats, leading to growth retardation (Allagui et al., 2014; Lukyanenko et al.,2013). Aluminum administration appears to lead to neurological (autism, encephalopathy, Alzheimer’s disease) and hematological (anemia) adverse effects regardless of the route of administration (Swegert et al., 1999).

Impact of aluminum and *Lactobacillus rhamnosus* on neurobehavioral tests

To evaluate the effect of AlCl3 and probiotic on the cognitive and neurobehavioral functions of rats, different neurobehavioral tests were proposed to assess anxiety, locomotor activity, memory, and depression.

Dark and Light Test

This test is used to determine the state of stress in rodents, knowing that they generally dislike lighted places. Thus, the more anxious the animal, the more its exploration will be reduced to the dark compartment (Zewed et al., 2018). The results obtained revealed that the animals intoxicated by AlCl3 tend to spend more time in the clear compartment during the 5 min of the test compared to the control animals ($p<0.001$), this gives a clear picture of its psychological state that the intoxicated rats live in a state of permanent stress due to a neurophysiological impairment (Liaquat et al., 2017). While the anti-anxiety effect was found in both treated and intoxicated rats treated after probiotic treatment, these results are in agreement with the new concept of psychobiotics (Dinan et al., 2013), (Figure 02).

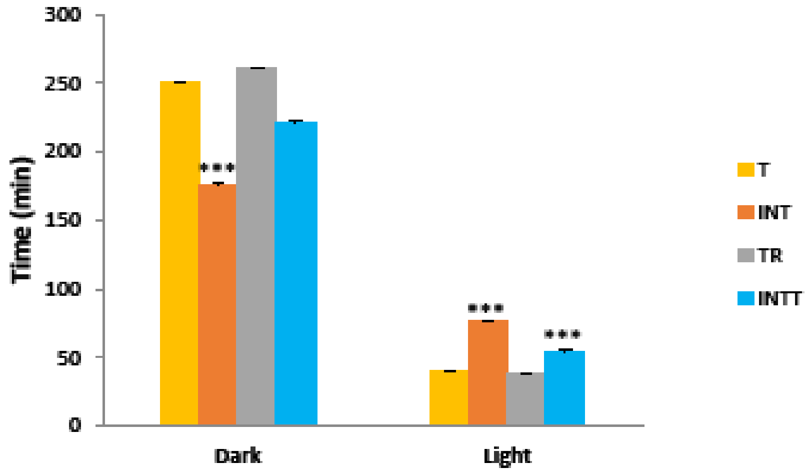

Figure 2. The time spent in the light compartment in the four lots. Values are expressed as mean ± SEM (***: p<0.001).

Locomotor activity (Open field)

The open field test results obtained from this study show a significantly (p<0.001) reduced number of tiles traversed by AlCl3 intoxicated rats compared to control rats as well as the number of visits to the center. The AlCl3-intoxicated rats show locomotor hypoactivity compared to control rats. This hypoactivity is due to altered signaling pathways between neurons as well as loss of synapses and neurons and decreased synthesis of neurotransmitters such as dopamine, glutamate, and serotonin (Liaquat et al., 2017). Increased toileting and defecation are a marker of stress (Sethi et al., 2008). These results agree with Rashwan et al. (2018) and show that the open field test reflects behavior related to exploratory activity and anxiety that are expressed in AlCl3-intoxicated rats by reduced horizontal and vertical exploratory activity, high latency, and high defecation. Exposition to AlCl3 induces significant alterations in a number of motor functions and an increase in motor neuron apoptosis (Gadouche et al., 2018). However, administration of probiotics resulted in a marked improvement in locomotor activity in both intoxicated and treated rats, as well as improvement in their exploratory and emotional states, suggesting that the probiotic helps support the nervous systems and may help release emotional blockages and bring a sense of balance. The same observations were made by Abildgaard et al (2017) who tested the anti-stress effect of eight probiotic strains on different adult rats, (Table 02).

Table 2. The different parameters measured during the locomotor activity test

Lots	Time of latency (Sec)	Number of panes crossed	Number of adjustment	Number of visits to the center	Number of grooming	Number of defecation
T	59,25±1,39	125,5±1,05	17,75±1,50	3,875±0,51	1,125±0,35	1,25±0,25
INT	119±0,96***	82,75±1,22***	10,375±0,70***	1,625±0,26**	2,875±0,39	1,75±0,31
TR	57,12±0.54	94.4±0,34	18,52±0,78	2,41±0,91	1,10±0,34	1,14±0,7
INTT	94±0,23***	87.63±1,21***	13.06±0.30**	2.16±0.27**	1.22±0.33	1.22±0.24

Values are expressed as mean ± SEM: (**: p<0.01; ***: p<0.001).

Three-arm maze test (Y-maze)

Y maze test used to assess short-term memory. The results show that the percentage of alternations and the number of visits is significantly lower in intoxicated rats compared to control rats (Fig 03).

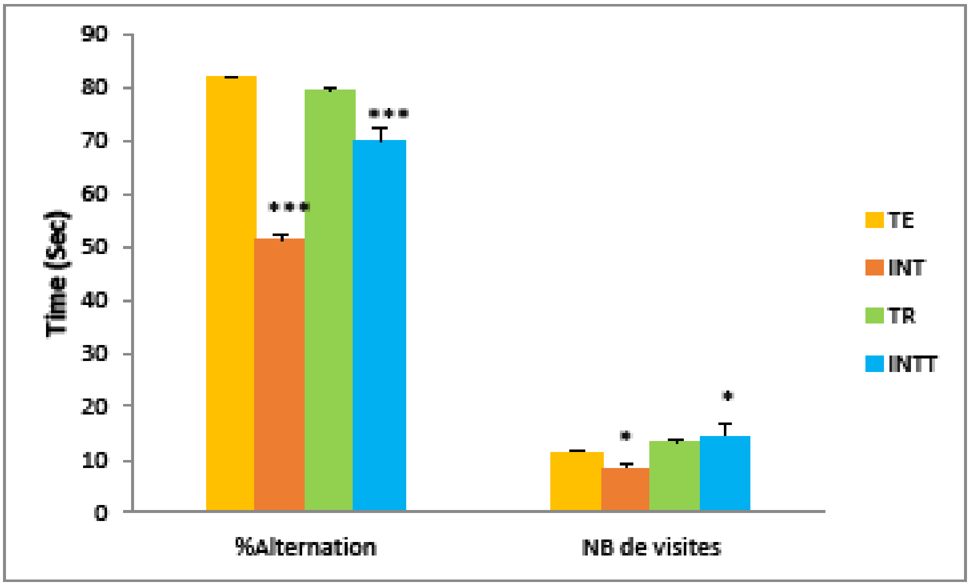

Figure 3. The percentage of alternation and number of visits in Control (TE), Treated (TR), AlCl3-intoxicated (INT), Treated Intoxicated (INTT) rats. Values are expressed as mean ± SEM: (***: $p<0.001$ *: $p<0.05$).

Our results agree with Cao et al (2017) and suggest that AlCl3 impairs working memory (short-term memory) where the percentage of alternations was reduced under the effect of this xenobiotic. AlCl3 causes behavioral, biochemical and pathological signs similar to that of Alzheimer's disease that manifest as losses of short-term memory and spatial working memory (Abdelghany et al.,2019). The results show that there is a significant increase in the percentage of alternation and the number of visits in the treated intoxicated rats compared to the rats intoxicated by AlCl3. According to the publication of Descoins, (2017) (National Institute of Agricultural Research), shows that intestinal bacteria influence our behaviors, regulating our emotional responses and intervene in these pathologies of the nervous system as well as the researchers revealed that the ingestion of the bacterium Lactobacillus farciminis (a lactic acid bacterium) can decrease in a non-negligible way the stress of rats. This probiotic restricts the permeability of the intestinal barrier and thus reduces the passage of lipopolysaccharides present in the intestines into the circulation. As the latter are incriminated in the induction of neuroinflammation in the brain, accentuating the effects of stress, the reduction of their passage would then be considered as an "anti-stress" effect.

Morris Pool Test

The Morris water maze test is commonly used to assess spatial memory in rodents. It was originally designed to test the ability of rats to learn and remember the position of a hidden platform in an opaque water pool relative to external cues. In agreement with Thenmozhi et al. (2015) and Iqbal et al. (2016), our results suggest that AlCl3-intoxicated rats took longer to reach the platform compared to control rats during the acquisition phase, and during the probe the intoxicated rats have a significantly lower latency in the NO frame compared to control rats (Fig 4,5 and 6).

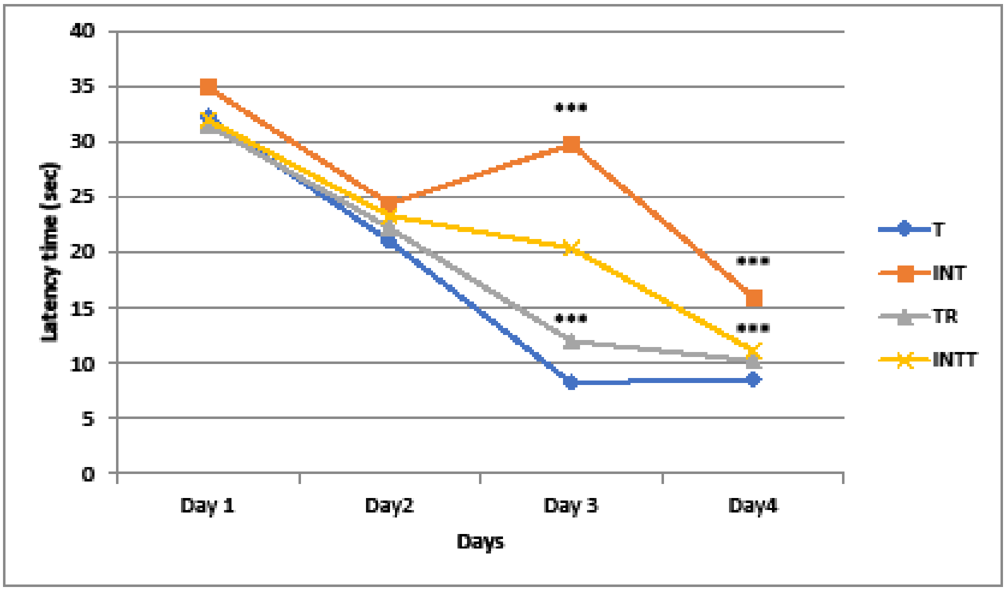

Figure 4. Morris pool test, latency during the learning phase (4 days) in control (TE), Treated (TR), Intoxicated (INT) and Intoxicated Treated (INTT) rats. Values are expressed as mean ± SEM: (***: $p<0.001$).

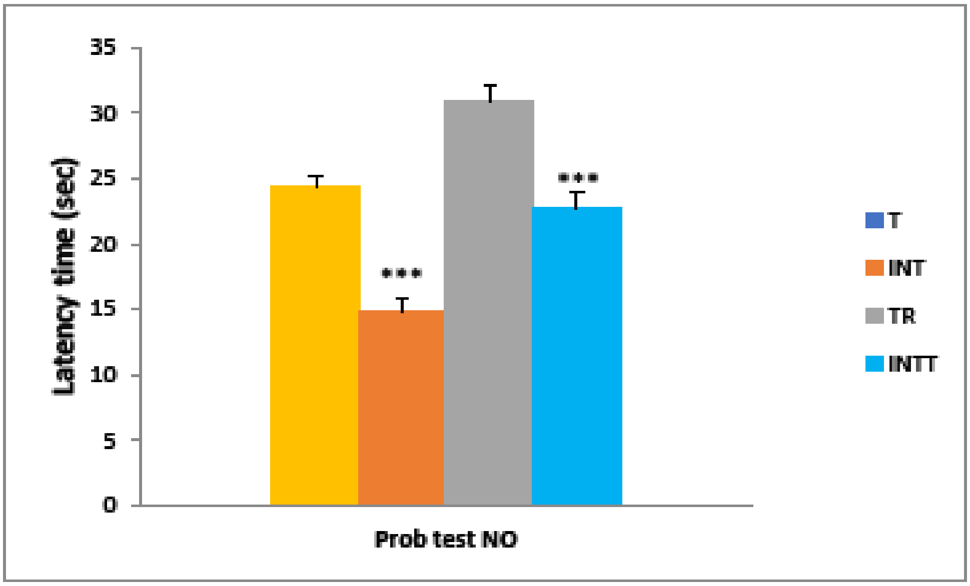

Figure 5. The time spent in frame (NO) during the probe test by Control (TE), Treated (TR), Intoxicated (INT), Intoxicated Treated (INTT) rats. Values are expressed as mean ± SEM: (***: $p<0.001$).

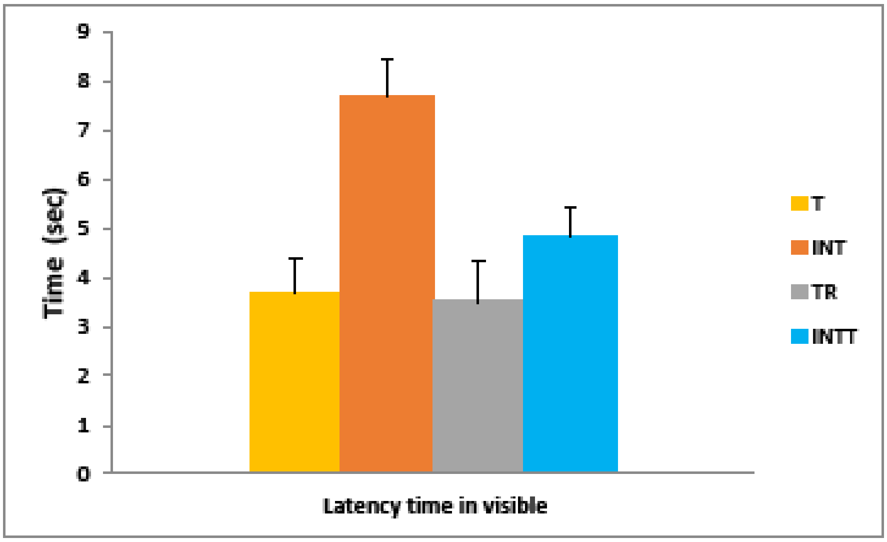

Figure 6. The latency time during the visible platform in Control (TE), Treated (TR), Intoxicated (INT) and Intoxicated Treated (INTT) rats. Values are expressed as mean ± SEM

Experiments have shown that the use of AlCl3 leads to a decrease in learning and memory capacity and to a dysfunction of cholinergic neurons. Acetylcholine (Ach) is an important neurotransmitter involved in learning and memory and can be increased in the hippocampus and cerebral cortex, it is synthesized by choline acetyltransferase (ChAT) and hydrolyzed by Acetylcholinesterase (AChE) (Xiao et al., 2011). AChE activity is sensitive to exogenous factors, including metals such as Al (Prema et al., 2016), it has been reported that Al3+ can interact with the peripheral sites of AChE and alter its secondary structure and ultimately increase its activity (Thenmozhi et al., 2015). Each AChE molecule degrades approximately 25,000 ACh molecules per second in all neuronal tissues (Prema et al., 2016). In parallel, the improvement of spatial memory in intoxicated and treated rats was well established in this work, by the decrease of latency during the acquisition phase and an increase of latency in the NW quadrant of the platform for the probe test. Based on these results, we hypothesize that probiotics can improve memory impairment induced by chronic aluminum intoxication in wistar rats, which is consistent with several works that have shown the activity of probiotic lactobacilli on the improvement of impaired memory (Woo et al., 2014).

Forced swimming test FST

For the forced swimming test, Rashwan et al (2018) found that this test was used to assess behavioral despair and depression in rodents. The recorded results show that there is a significant increase ($p<0.001$) in the time of immobility (TIM) in AlCl3 intoxicated rats compared to control rats (Fig 07) which is considered an index of depression-like behavior that results in a chronic stress state. Our results are consistent with Rebai and Djebli (2008) and suggest that exposure to 50 mg/kg AlCl3 for 12 weeks increases this immobility time in intoxicated rats and that antidepressant activity is related to immobility time in this test. Lin et al (2015) found that reduced motility time is an indicator of increased depressive state (behavioral hopelessness), indicating disruption of serotonergic neurotransmission. On the other hand, the decrease in MIT in treated rats reflects the positive effect of probiotacin on despair behavior which is explained that probiotics could attenuate depressive behavior according to Arseneault-Bréard et al., (2012).

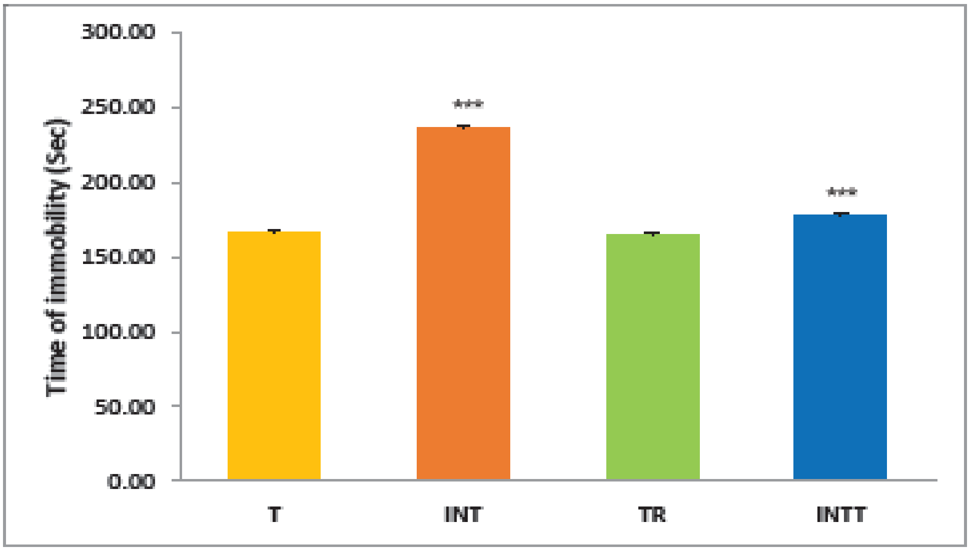

Figure 7. The time of immobility during the forced swimming test in Control (TE), Treated (TR), Intoxicated (INT) and Intoxicated Treated (INTT) rats. Values are expressed as mean ± SEM: (***: $p<0.001$).

Impact of aluminum and *Lactobacillus rhamnosus*on hematological parameters

Hematological parameters are generally used for the determination of inflammation and infections, therefore, the results of FNS (blood count formula) revealed a significant decrease in hemoglobin level (HGB $p<0.001$) and hematocrit percentage (HTC $p<0.01$) in AlCl3 intoxicated rats compared to that of control rats (Table 03).

Table 03: Evaluation of hematological parameters in control, AlCl3 intoxicated, treated and probiotic treated intoxicated rats.

Lots	WBC.10^3/mm^3	GR.10^6/mm^3	HGB g/dl	PLT.10^3/mm^3	HCT %
T	5,425 ± 0,06	8,265 ± 0,17	15,775 ± 0,17	321 ± 3,55	43,725 ± 0,57
INT	4,075±0,04**	7,765±0,04***	14,125±0,06***	448±9,17***	41,35±0,23**
TR	9,27±0.91	8,234±2,46	14.98±5.8	313±5.18	42.65±0.48
INTT	7,55±0.29***	7.901±0.22**	14.54±9.1**	402.5±3.71**	41.72±0.19

Values are expressed as mean ± SEM (***: $p<0.001$; **: $p<0.01$).

the decrease in hemoglobin levels results in the appearance of hypochromic iron deficiency and microcytic anemia (Gourier-Fréry et al., 2004). Also, the hematological study showed that the number of white blood cells (WBC) in the intoxicated rats was lower than in the control rats. Al by its action on the defense mechanisms related to WBCs and macrophages (categories of WBCs that have a phagocytosis function: capture and ingestion of particles foreign to the body). Thus, these macrophages, which typically clear amyloid plaque accumulations in healthy individuals, fail to do so in Alzheimer's disease (Douichene, 2015). On the other hand, it was noticed that these different hematological abnormalities are corrected by the administration of the probiotic strain. This is reflected by its regulatory power of RBC, hemoglobin and platelets (Shokryazdan et al., 2016). However, the high number of WBCs indicates either the speed of growth of the probiotic strain resulting in the rapid invasion of the gastrointestinal tract by a new bacterial strain that generates an immune response or the presence of an infection of the body by a pathogenic species. After the administration of the probiotic strain in AlCl3 intoxicated rats, we noticed a significant increase in the number of white blood cells (WBC $p<0.001$), red blood cells (RBC $p<0.01$), as well as the hemoglobin level (HGB $P<0.01$) and for the percentage of HCT we did not record a significant difference between the treated intoxicated rats and the intoxicated rats. On the other hand, the recorded results show a significant decrease in the number of platelets (PLT) in the treated intoxicated rats compared to the AlCl 3 intoxicated rats ($p<0.01$). In normal human serum, Al binds 60% to transferrin, and 34% to albumin, and the remainder mainly to citrate. When Al binds to transferrin, it takes the place of iron, which is no longer transported to the parts of the body that need it. In Alzheimer's disease and Down syndrome, transferrin is no longer able to bind Al properly. This is due to a mutation in the gene that codes for transferrin. This gene then codes for an abnormal mutated transferrin, transferrin C2 (Tf C2). This C2 transferrin binds poorly with iron and Al. These two metals, not sufficiently bound to transferrin, thereby generate free radicals that damage cell membranes (Boutaleb, 2017). Moreover, the iron and Al present in the brain cannot take advantage of this mutated transferrin to leave and thus leave in the bloodstream. These two metals are therefore deposited in the nervous tissue and accumulate there. Al also attacks all blood cells: red blood cells, white blood cells, blood platelets (Osinska et al., 2004; Kaizer et al., 2007). The anemia seen in Al-intoxicated rats is explained by the interference of Al in iron metabolism and the toxic action of Al on the erythroblast lineage (Gonzalez et al., 2000; Mahieu et al., 2000). This creates a microcytic type of anemia due to iron deficiency. But Al can also directly attack the walls of red blood cells, making them fragile, inducing their apoptosis, causing them to burst and creating a hemolytic type anemia (Bulat et al., 2008; Bazzoni et al., 2005; Farina et al., 2005; Niemoeller et al., 2006). Al can make alterations in all tissues of the body (Douichène et al., 2016).

Impact of aluminum and *Lactobacillus rhamnosus*on biochemical parameters

biochemical parameters are used to detect organ-related problems (Petterino and Argentino, 2006).

Blood sugar

The results of the blood glucose assay showed that there is a significant increase in $AlCl_3$ intoxicated rats compared to control rats ($p<0.001$), (Figure 08).

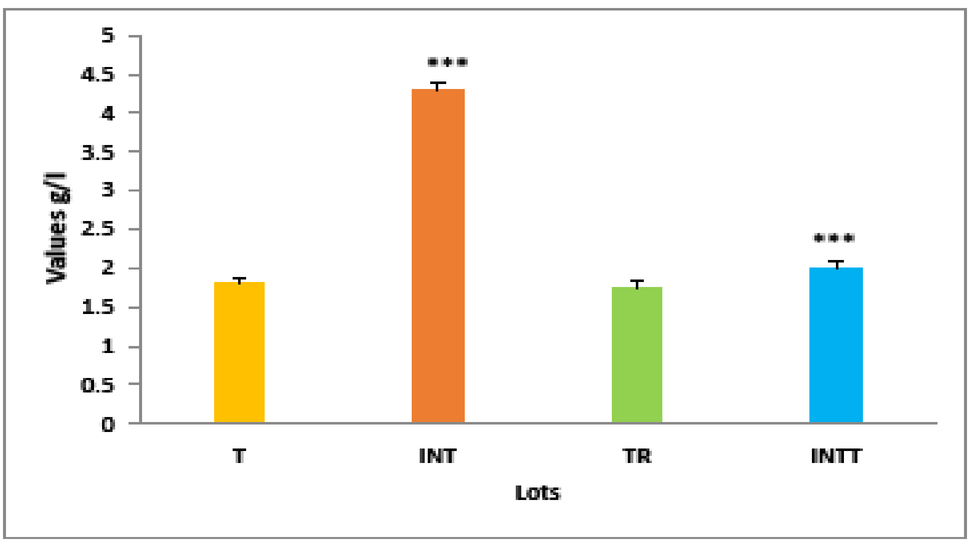

Figure 8. The blood glucose determination in Control (TE), Treated (TR), Intoxicated (INT) and Intoxicated Treated (INTT) rats. Values are expressed as mean ± SEM: (***: $p<0.001$).

which in agreement with the results of Belaïd et al (2012). The increase in blood glucose concentration is probably the result of glycogen degradation (glycogenolysis at the hepatic level), the hyperglycemia would be directly related to the adverse effects of aluminum on the pancreas and more exactly on insulin secretion by the islets of langerhans (Saka et al., 2011; Behadada, 2017). On the other hand, treatment with probiotic in AlCl3 intoxicated rats gave a significant decrease in blood glucose level in comparison with AlCl3 intoxicated rats (p<0.001). This was shown that this probiotic has hypoglycemic activity by regulation of energy metabolism.

Exploration of the hepatic function

The liver is an essential organ, the site of bioaccumulation of most xenobiotics, and transaminases are intracellular enzymes, released into the bloodstream after hepatocyte damage and necrosis. Our results indicate that serum ALAT and ASAT activity is significantly higher in AlCl3 intoxicated rats compared to control rats (p<0.001), (Table 04).

Table 4. Effect of probiotic on liver enzyme activity and bilirubin content in AlCl3-intoxicated rats compared to control rats.

	T	INT	TR	INTT
ALT (UI/l)	47,02 ±0,59	81,9 ±0,62***	49,33 ±0,42	50 ±0,11***
AST (UI/l)	100 ±0,55	256 ±0,5***	99,7 ±0, 34	182,5±3,10***
Total bilirubin (mg/l)	0,84 ±0,05	2,05 ±0,01**	0,79±0,06	1,21±0,03**

Values are expressed as mean ± SEM: (***: p<0.001;**: p<0.01).

which may be a sign of impaired liver function. The possible mechanism of the observed elevation in transaminases may be due to liver dysfunction and disturbances in the biosynthesis of these enzymes which are indicators for liver damage and thus functional liver failure (Boutaleb et al., 2017). As well as the total bilirubin parameter is significantly elevated in AlCl3 intoxicated rats compared to control rats (p<0.01). Our results, in agreement with those of Gonzalez et al (2008), reflect a significant increase in total bilirubin in AlCl3 intoxicated rats compared to control rats. This hyperbilirubinemia due to the accumulation of this metal as well as its toxicity in the liver tissue. Sedlak and Snyder, (2004) found that elevated serum bilirubin is associated with either free radical production or periportal necrosis. Moreover, the administration of the probiotic strain to AlCl3 intoxicated rats illustrates a significant decrease in the serum value of total bilirubin in comparison with AlCl3 intoxicated rats (p<0.01). These results showed the regulatory effect of probiotics on the different liver functions, which was well observed by the work of Gu et al (2019), who noticed that the administration of *Lactobacillus rhamnosus* capsules at different doses (low, medium and high) in mice, significantly reduced liver damage by reducing the accumulation of triglycerides and free fatty acids, and the inflammatory response in the liver.

Determination of lipids

Statistical analysis reveals that plasma lipid content mainly triglycerides and total cholesterol are significantly higher (p<0.001) in AlCl3 intoxicated rats compared to control rats (Fig 09).

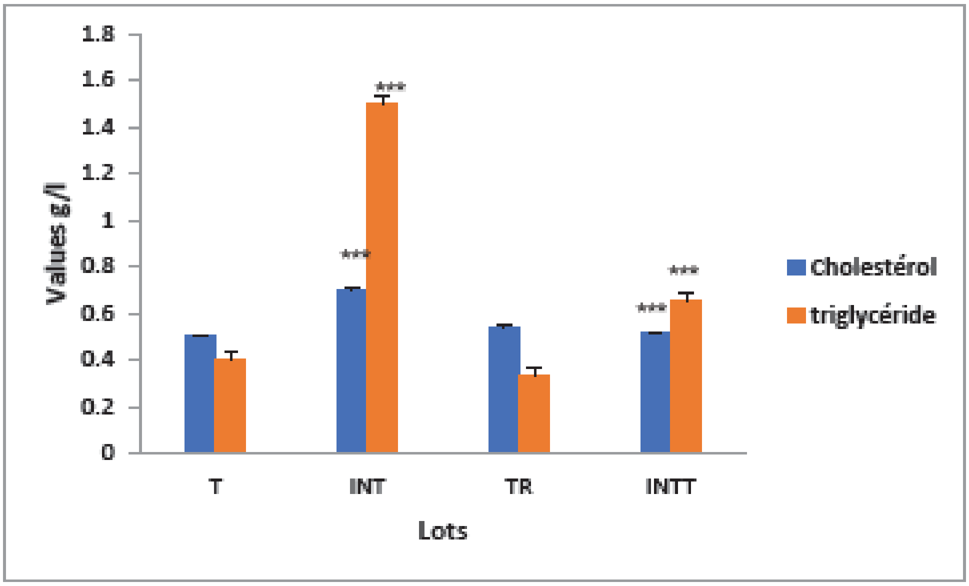

Figure 9. Plasma lipid content in intoxicated rats compared to control rats. Values are expressed as mean ± SEM: (***: p<0.001)

This indicates a loss of plasma membrane integrity has a significant effect on the various membrane bound enzymes in terms of alterations in ALAT and ASAT enzymatic activity and also an accumulation of this metal in the liver, this can lead to disturbances in lipid metabolism, also Al has a strong affinity for phosphate groups and binds to the head of phospholipids by electrostatic forces, which can induce conformational changes in the lipid bilayer of the plasma membrane. Moreover, the consumption of probiotic bacteria probably contributes to the reduction of lipidic compounds evaluated in this experiment, thus confirming the results obtained by Mahdavi et al. (2005) and Idoui (2008) who also noted a hypocholesterolemic and hypotriglyceridemic activity in animals having consumed probiotics. Probiotics act on cholesterol either by a direct lipolytic activity or by modifying the metabolism of bile salts and cholesterol. Hypotheses for this phenomenon include the production of an inhibitor of an enzyme involved in cholesterol synthesis (orotic acid) and the absorption of cholesterol by lactic acid bacteria itself is another hypothesis to consider (Amara, 2012).

Exploration of the kidney function

The kidneys are vital organs that perform major functions such as blood purification and hormone secretion. The biochemical results of renal biomarkers at the end of the experiment showed a significant elevation of urea and creatinine in $AlCl_3$ intoxicated rats compared to control rats (p<0.001; p<0.01 respectively), (Table 05).

Table 5. The different parameters of renal function in Control (TE), Treated (TR), Intoxicated (INT) and Intoxicated Treated (INTT) rats

	T	INT	TR	INTT
Creatinine (mg/dl)	7,87 ±006	12,49 ±002*	7,48 ±001	10,65 ±004*
Urea (g/l)	0,23 ±0,06	0,86 ±0,03**	0,25 ±0,05	0,30 ±0,04**

Values are expressed as mean ± SEM: ***: p<0.001; **: p<0.01).

This is similar with the results of Boutaleb et al. (2017). This elevation is an important marker of renal dysfunction and the inability of the kidneys to filter the blood of these toxic wastes (Mahieu et al., 2005). However, administration of the probiotic strain in AlCl3 intoxicated rats causes a significant decrease in urea and creatinine compared to AlCl3 intoxicated rats ($p<0.001$; $p<0.05$) respectively, the same results were reported by Shokryazdan et al (2016), on a model of rats treated with two different strains of *L. buchneri* FD2 and *L. fermentum* HM3 and showed an improvement in renal function by decreasing urea and creatinine levels. In agreement with Boutaleb et al, (2017).

Conclusion

Our work has shown that the beneficial effect of the probiotic strain (*Lactobacillus rhamnosus*) against aluminium intoxication in wistar rats results in an improvement of the different neurobehavioural tests (anti-anxiety and antidepressant effect; positive effect of learning and memorization); and a correction of the parameters of the renal function (uric acid, creatinine) and the hepatic function (ALT, ASAT) as well as the hematological parameters.

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References

Abdelghany, AK, Khalil, F, Azeem, NMA, El-Nahass, ES, El-Kashlan, AM, Emeash, HH (2019). Ginseng and moringa olifera ameliorated cognitive impairments induced by aluminium chloride in albino rat. Adv. Anim. Vet. Sci 7(7): 557-565.

Abdulmalek, S, Suliman, M, Omer, O (2015). Posssible neuroprotective role of Pomegranate Juice in Aluminium Chloride induced Alzheimer's like disease in mice. Alzheimer's Disease and Parkinsonism 5: 188.

Abildgaard, A, Elfving, B, Hokland, M, Wegener, G, Lund, S (2017). Probiotic treatment reduces depressive-like behaviour in rats independently of diet. Psychoneuroendocrinology 79: 40-48.

Ait-Belgnaoui, A, Han, W, Lamine, F, Eutamene, H, Fioramonti, J, Bueno, L, Theodorou, V (2006). *Lactobacillus farciminis* treatment suppresses stress induced visceral hypersensitivity: a possible action through interaction with epithelial cell cytoskeleton contraction. Gut 55(8) : 1090-1094.

Allagui, MS, Feriani, A, Saoudi, M, Badraoui, R, Bouoni, Z, Nciri, R, Elfeki, A (2014). Effects of melatonin on aluminium-induced neurobehavioral and neurochemical changes in aging rats. Food and chemical toxicology 70: 84-93.

Amara, S, Zadi-Karam, H, & Karam, NE (2019). Selection of Lactobacillus strains newly isolated from Algerian camel and mare fermented milk for their in vitro probiotic and lipolytic potentials. African Journal of Biotechnology 18(30): 882-894.

Arseneault-Bréard, J, Rondeau, I, Gilbert, K, Girard, SA, Tompkins, TA, Godbout, R, Rousseau, G (2012). Combination of Lactobacillus helveticus R0052 and Bifidobacterium longum R0175 reduces post-myocardial infarction depression symptoms and restores intestinal permeability in a rat model. British Journal of Nutrition 107(12): 1793-1799.

Bahri, F, Chaouche, NK (2016). Partial characterization of bacteriocin-like substance produced by probiotic Lactobacillus plantarum F12 isolated from Algerian children faeces. African Journal of Microbiology Research 10(43): 1798-1805.

Bazzoni, GB, Bollini, AN, Hernández, GN, del Carmen Contini, M, Chiarotto, MM, Rasia, ML (2005). In vivo effect of aluminium upon the physical properties of the erythrocyte membrane. Journal of inorganic biochemistry 99(3): 822-827.

Behadada, O, Abi-Ayad, M, Kontonatsios, G, & Trovati, M (2017). Automatic Diagnosis Metabolic Syndrome via a $$ k-$$ Nearest Neighbour Classifier. In *International Conference on Green, Pervasive, and Cloud Computing* (pp. 627-637). Springer, Cham.

Belaïd-Nouira, Y, Bakhta, H, Bouaziz, M, Flehi-Slim, I, Haouas, Z, & Cheikh, HB (2012). Study of lipid profile and parieto-temporal lipid peroxidation in AlCl 3 mediated neurotoxicity. Modulatory effect of fenugreek seeds. Lipids in health and disease 11(1): 1-8.

Benreguieg, M, Dalache, F, Gacemi, B (2013). Characterization of antibacterial activity and potential as probiotic of lactic acid bacteria isolated from goat's milk in Algeria. Journal of Life Sciences 7(8): 802.

Berihu, BA, Afwerk, M, Debeb, YG, Gebreslassie, A (2015). Review on histological and functional effect of aluminium chloride on cerebral cortex of the brain. International Journal of Pharmacology Sciences and Research 6: 1105-1116.

Boutaleb, A, Saoula,H, Aissaoui, M, Hamidouche, D, Aissat, Y, Mahiou, H, Osmane, R, Zmiri, Y, Mitiche, A (2017). Celiac disease and inflammatory bowel disease, a rare association. J. of crohns & collitis 11: S181-S181.

Bulat, P, Potkonjak, B, Đujić, I (2008). Lipid peroxidation and antioxidative enzyme activity in erythrocytes of workers occupationally exposed to aluminium. Arhiv za higijenu rada i toksikologiju 59(2): 81-87.

Cao, Z, Wang, F, Xiu, C, Zhang, J, Li, Y (2017). Hypericum perforatum extract attenuates behavioral, biochemical, and neurochemical abnormalities in Aluminum chloride-induced Alzheimer's disease rats. Biomedicine & pharmacotherapy 91 : 931-937.

Coudeyras, S, Forestier, C (2010). Microbiote et probiotiques: impact en santé humaine. Canadian Journal of Microbiology 56(8): 611-650.

Crawley, J, Goodwin, FK (1980). Preliminary report of a simple animal behavior model for the anxiolytic effects of benzodiazepines. Pharmacology Biochemistry and Behavior 13(2): 167-170.

Dauge, V, Rpssignol, P, Roques, BP (1989). Comparison of the behavioural effects induced by administration in rat nucleus accumbens or nucleus caudatus of selective mu and delta opioid peptides or kelatorphan, an inhibitor of enkephalinmetabolism. Psychopharmacology 96 : 343-352.

Descoins, L (2017). Microbiote et cerveau: corrélation avec les pathologies neurologiques et psychiatriques (Doctoral dissertation, Université Toulouse III-Paul Sabatier).

Dinan, TG, Stanton, C, Cryan, JF (2013). Psychobiotics: a novel class of psychotropic. Biological psychiatry 74(10) : 720-726.

Douichene, S, Hammadi, K, Djebli, N (2016). Neuroprotective Effect of Hypericum thymopsis Against Chronic Exposure to Aluminum Chloride and Alzheimer's Disease. Journal of Pharmacy and Pharmacology 3(3): 20-28.

Douichene, S, Rached, W, Djebli, N (2020). Hepato-Protective Effect of Curcuma longa against Paracetamol-Induced Chronic Hepatotoxicity in Swiss Mice. Jordan Journal of Biological Sciences 13(3).

El-Nahrery, EMA (2015). « Vitamin E protect against neurotoxicity on rat model of Alzheimer's disease ». World Journal of Pharmaceutical Research 4 :124-140.

Farina, M, Rotta, LN, Soares, FAA, Jardim, F, Jacques, R, Souza, DO, Rocha, JBT (2005). Hematological changes in rats chronically exposed to oral aluminum. Toxicology 209(1): 29-37.

Gadouche, L, Djebli, N, Zerrouki, K (2018). Pomegranate juice attenuates neurotoxicity and histopathological changes of the nervous system induced by aluminum in mice. Phytothérapie 16(3): 133-141.

González-Muñoz, MJ, Pena, A, Meseguer, I (2008). Role of beer as a possible protective factor in preventing Alzheimer's disease. Food and Chemical Toxicology 46(1): 49-56.

González-Revaldería, J, Casares, M, Paula, MD, Pascual, T, Giner, V, Miravalles, E (2000). Biochemical and hematological changes in low-level aluminum intoxication. Clin Chem Lab Med 38(3): 221-225.

Gourier-Frery, C, Frery, N, Berr, C, Cordier, S (2003). Aluminium. Quels risques pour la santé ? Volet épidémiologique de l'expertise collective/Evaluation des risques sanitaires liés l'exposition de la population française à l'aluminium ». Invs-Afssap. Paris. p 1253.

Gupta, VB, Anithaa, S, Hegdea, ML, Zeccab, L, Garrutoc, RM, Ravidd, R, Shankare, SK, Steinf, R, Shanmugavelug, P, Raoa, KS (2005). Aluminum in Alzheimer's disease: are we still at a crossroad? . CMLS, Cell. Mol. Life Sci 62: 143–158.

Idoui, T, Karam, NE (2008). Lactic acid bacteria from Jijel's traditional butter: Isolation, identification and major technological traits. Grasas y Aceites 59(4): 361-367.

Iqbal, G, Iqbal, A, Mahboob, AM, Farhat, S, Ahmed, T (2016). Memory enhancing effect of black pepper in the AlCl3 induced neurotoxicity mouse model is mediated through its active component chavicine. Current pharmaceutical biotechnology 17(11): 962-973.

Kaplan A. Urea. Kaplan A et al, 1984. ClinChem The C.V. Mosby Co. St Louis. Toronto. Princeton 1261-1266 and 418.

Karbouj, R, Desloges, I, Nortier, P (2009). A simple pre-treatment of aluminium cookware to minimize aluminium transfer to food. Food and chemical toxicology 47(3): 571-577.

Kesarcodi, AW, Kaspar, H, Lategan, G, Gibson, L (2008). Probiotics in aquaculture: The need, principles and mechanisms of action and screening processes ». Aquaculture

274: 1–14.

Liaquat, L, Muddasir, S, Batool, Z, Khaliq, S, Tabassum, S, Emad, S, Haider, S (2017). Development of AD like symptoms following co-administration of AlCl3 and D-gal in rats: A neurochemical, biochemical and behavioural study. Pakistan journal of pharmaceutical sciences 30 (2): 647.

Lin, SH, Chou, ML, Chen, WC, Lai, YS, Lu, KH, Hao, CW, Sheen, LY (2015). A medicinal herb, Melissa officinalis L. ameliorates depressive-like behavior of rats in the forced swimming test via regulating the serotonergic neurotransmitter. Journal of ethnopharmacology 175: 266-272.

Lukyanenko, LM, Skarabahatava, AS, Slobozhanina, EI, Kovaliova, SA, Falcioni, ML, Falcioni, G (2013). In vitro effect of AlCl3 on human erythrocytes: changes in membrane morphology and functionality. Journal of Trace Elements in Medicine and Biology 27(2): 160-167.

Mahdavi, AH, Rahmani, HR, Pourreza, J (2005). Effect of probiotic supplements on egg quality and laying hen's performance. Int. J. Poult. Sci 4(7) : 488-492.

Mahieu, S, del Carmen, CM, Gonzalez, M, Millen, N, Elias, MM (2000). Aluminum toxicity. Hematological effects. Toxicology letters 111(3): 235-242.

Mahieu, S, Millen, N, González, M, del Carmen, CM, Elías, MM (2005). Alterations of the renal function and oxidative stress in renal tissue from rats chronically treated with aluminium during the initial phase of hepatic regeneration. Journal of inorganic biochemistry 99(9): 1858-1864.

Mahmoudi, F, Hadadji, M, Benlahcen, K (2015). SAFETY AND PROTECTIVE EFFECT OF BIFIDOBACTÉRIUM SPP. USED AS PROBIOTIC AGENT IN VIVO AGAINST ENTEROPATHOGENIC ESCHERICHIA COLI. Innov. Rom. Food Biotechnol 16: 37-41.

Misslin, R, Belzung, C, Vogel, E (1989). Behavioural validation of a light/dark choice procedure for testing anti-anxiety agents. Behavioural processes 18(1-3): 119-132.

Morris, R (1984). Developments of a water-maze procedure for studying spatial learning in the rat. Journal of neuroscience methods 11(1): 47-60.

Murray R.L. Creatinine. Kaplan a et al, 1984. ClinChem The C.V. Mosby Co. St Louis. Toronto. Princeton 1261-1266 and 418. Mesure de l'activité des enzymes antioxydants.

Niemoeller, OM, Kiedaisch, V, Dreischer, P, Wieder, T, Lang, F (2006). Stimulation of eryptosis by aluminium ions. Toxicology and applied pharmacology 217(2): 168-175.

Nimgampalle, M, Kuna, Y (2017). Anti-Alzheimer Properties of Probiotic, Lactobacillus plantarum MTCC 1325 in Alzheimer's Disease induced Albino Rats ». Journal of Clinical and Diagnostic Research 11(8): 5.

Petterino, C, Argentino-Storino, A (2006). Clinical chemistry and haematology historical data in control Sprague-Dawley rats from pre-clinical toxicity studies. Experimental and Toxicologic Pathology 57(3): 213-219.

Porsolt, RD, Le Pichon, M, Jalfre, ML (1977). Depression: a new animal model sensitive to antidepressant treatments. Nature 266(5604): 730-732.

Prema, A, Thenmozhi, AJ, Manivasagam, T, Essa, MM, Akbar, MD, Akbar, M (2016). Fenugreek seed powder nullified aluminium chloride induced memory loss, biochemical changes, Aβ burden and apoptosis via regulating Akt/GSK3β signaling pathway. PLOS one 11(11): e0165955.

Prieur, EA, Jadavji, NM (2019). Assessing spatial working memory using the spontaneous alternation Y-maze test in aged male mice. Bio-protocol 9(3).

Ramdane, MS, Guitarini, DJ (2008). Effets des probiotiques sur 3 germes de la flore intestinale poulet de chair ». Bulletin UASVM, Horticulture 65(2): 614-620.

Rashwan, EH, Kamel, MM, El-lethey, HS, Ciobica, A, El Iraqi, KG, Ahmed-Farid, OA (2018). Caffeine Ameliorating Effect on Anxiety and Depression in an Aluminum Chloride-induced Alzheimer's Disease Rat Model. International Journal of Pharmaceutical Research & Allied Sciences 7(3).

Rebai, O, Djebli, NE (2008). Chronic exposure to aluminum chloride in mice: exploratory behaviors and spatial learning. Adv Biol Res 2(1-2): 26-33.

Rivière, P (2020). Maladies inflammatoires chroniques de l'intestin de l'adulte et microbiote. Côlon & Rectum 14(2): 74-79.

Saka, HA, Thompson, JW, Chen, YS, Kumar, Y, Dubois, LG, Moseley, MA, Valdivia, RH (2011). Quantitative proteomics reveals metabolic and pathogenic properties of Chlamydia trachomatis developmental forms. Molecular microbiology 82(5): 1185-1203.

Sanchez-Iglesias, S, Soto-Otero, R, Iglesias-Gonzalez, J, Barciela-Alonso, MC, Bermejo-Barrera, P, Mendez-Alvare, E (2007). Analysis of brain regional distribution of aluminium in rats via oral and intraperitoneal administration. J. Trace Elem. Med. Biol 21:31-34.

Sedlak, TW, Snyder, SH (2004). Bilirubin benefits: cellular protection by a biliverdin reductase antioxidant cycle. Pediatrics 113(6): 1776-1782.

Sethi, P, Jyoti, A, Singh, R, Hussain, E, Sharma, D (2008). Aluminium-induced electrophysiological, biochemical and cognitive modifications in the hippocampus of aging rats. Neurotoxicology 29(6): 1069-1079.

Shokryazdan, P, Faseleh Jahromi, M, Liang, JB, Kalavathy, R, Sieo, CC, Ho, YW (2016). Safety assessment of two new Lactobacillus strains as probiotic for human using a rat model. PLoS One 11(7): e0159851.

Swegert, CV, Dave, KR, Katyare, SS (1999). Effect of aluminium-induced Alzheimer like condition on oxidative energy metabolism in rat liver, brain and heart mitochondria. Mechanisms of ageing and development 112(1): 27-42.

Thenmozhi, AJ, William Raja, TR, Janakiraman, U, Manivasagam, T (2015). «Neuroprotective effect of Hesperidin on Aluminium Chloride induced Alzheimer's disease in wistar rats». Neurochem Res 40 :767-776.

Thomas, C, Thomas, L (1992). Labor diagnostik v on Erkrankung en der Nier en und ableitendenHar (hrsg)Dans: Thomas L, 6 éd. Philadelphi, Labor und Diagnose.

Wanchai, K, Yasom, S, Tunapong, W, Chunchai, T, Eaimworawuthikul, S, Thiennimitr, P, Chattipakorn, N, Lungkaphin, A (2018). Probiotic Lactobacillus paracasei HII01 protects rats against obese-insulin resistance-3 induced kidney injury and impaired renal organic anion transporter 3 (Oat3) function». Clinical Science. 52p.

Wang, Z, Wei, X, Yang, J, Suo, J, Chen, J, Liu, X, Zhao, X (2016). Chronic exposure to aluminum and risk of Alzheimer's disease: A meta-analysis. Neuroscience letters 610 : 200-206.

Woo, JY, Gu, W, Kim, KA, Jang, SE, Han, MJ, Kim, DH (2014). «Lactobacillus pentosus var. plantarum C29 ameliorates memory impairment and inflammaging in a D-galactose-induced accelerated aging mouse model». Anaerobe 27: 22-26.

Xiao, F, Li, XG, Zhang, XY, Hou, JD, Lin, LF, Gao, Q, Luo, HM (2011). Combined administration of D-galactose and aluminium induces Alzheimerlike lesions in brain. Neuroscience Bulletin 27(3): 143-155.

Zewde, AM, Yu, F, Nayak, S, Tallarida, C, Reitz, AB, Kirby, LG, Rawls, SM (2018). PLDT (planarian light/dark test): an invertebrate assay to quantify defensive responding and study anxiety-like effects. Journal of neuroscience methods 293: 284-288.

التأثير الوقائي لسلالة بروبيوتيك *Lactobacillus Rhamnosus* ضد التسمم الناجم عن كلوريد الألومنيوم في فئران ويستار: دراسات دموية سلوكية-عصبية وكيميائية

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المُستَخلَص

الهدف: يعتبر الألمنيوم بأشكاله المختلفة من المواد كيميائية المضرة للبيئية حيث تشكل تهديدات كبيرة للصحة العامة. أثبتت الكائنات الحية المجهرية المعروفة باسم بروبيوتيك تأثيرات وقائية مهمة ضد السمية الخلوية الألومنيوم ALCL3. من أجل ذلك، تهدف الدراسة الحالية إلى تقييم اضطراب العوامل السلوكية العصبية والكيميائية الحيوية الدموية الناجمة عن التعرض المزمن للألمنيوم وكذلك التأثيرات الوقائية التي تمارسها البكتيريا اللبنية *Lactobacillus rhamnosus* عند ذكور الجرذان من نوع ويستر.

الطريقة: تم استعمال اثنان وثلاثين حيوانا تم تقسيمها إلى أربع مجموعات: المجموعة الأولى كانت بمثابة شاهد كما تلقت المجموعة الثانية 100 مليغرام للكيلوغرام من الألمنيوم .... لمدة 12 أسبوعا، فيما أخذت المجموعة الثالثة 10 مليلتر من السلالة البكتيرية على شكل محلول يحتوي على مائة مليون خلية في المليلتر الواحد لمدة أربع أسابيع، وأما المجموعة الرابعة فعرضت إلى نفس جرعة الألمنيوم لمدة 12 أسبوعا ثم البروبيوتيك لمدة 4 أسابيع.

النتائج: استعمال الألمنيوم قد أدى إلى انخفاض في وزن جسم الحيوان وكذلك وزن الدماغ مقارنة بالشاهد. كما أظهرت النتائج التي تم الحصول عليها اضطرابا معنويًا وسلوكًا شبيهًا بالقلق في الحيوانات المسممة، مع اضطراب في الؤشرات الكيميائية الحيوية الدموية المختبرة، خاصة منها الكلوية والكبدية.

الاستنتاج: بشكل عام، حال استخدام البروبيوتيك دون ظهور السلوك الشبيه بالاكتئاب الناجم عن الألمنيوم لدى الجرذان المتلقية للعلاج كما عرفت معظم المؤشرات الحيوية تعديلات معتبرة لقيمها مقارنة بالمجموعات المسممة وغير المعالجة. وعليه فإن البروبيوتيك يمكن اقتراحه كعلاج بديل للتسممات الناجمة عن الألمنيوم.

الكلمات المفتاحية: AlCl3، البروبيوتيك، *Lactobacillus rhamnosus*، الاختبارات السلوكية، البارامترات الكيميائية الحيوية للدم.