

## **Preventive Effect of Antioxidant, Curcumin, Against Formaldehyde-Induced Neurotoxicity in Rats**

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### **ABSTRACT**

Our problem is to evaluate the behavioral effects of infection and combination toxicity - infection in adult Wistar rats and the protective effect of an antioxidant (the curcumin) on neurobehavioral alterations and complications. Toxicity was induced by a single intraperitoneal injection of Formaldehyde (FA) at a dose of 10 mg/kg.

The administration of Formaldehyde which is revealed, on one hand, the effects of a single intra-peritoneal injection on anxiety behaviors and the other hand the protective role of antioxidant (curcumin) on FA-induced disorders. Behavioral test in the open field (OF) revealed that animals treated with FA exhibited an anxious behavior and an alteration in locomotive and exploratory activities when compared to control. The curcumin, a natural antioxidant was administered orally (gastric gavages) at a dose of 60 mg / kg. This administration reduces anxiety and the therapeutic benefits of curcumin against the deficits caused by formaldehyde.

**Key words:**-Neurotoxicity, Formaldehyde, Anxiety, Curcumin, Antioxidant

### **Introduction**

Epidemiological studies showed that long-term exposure of people to formaldehyde in the air might contribute to a series of neuropsychiatric symptoms, such as; depression, anxiety, sleep disturbances, malaise, balance dysfunctions, headaches, indigestion, lethargy, decreased motor activity, and loss of appetite [1]. Formaldehyde, a colourless liquid with strong hydrophilic characteristics and odour, is commonly used in medicine and industry [2]. After introduced into the organism, formaldehyde is converted into formic acid in the liver and

erythrocytes by the catalytic activity of formaldehyde dehydrogenase and affects individuals' quality of life and predispose them to psychiatric comorbidities. Depression is a consequence of anxiety, affecting 21% of populations [3].

Many natural products have interesting pharmacological effects and that they can represent a valuable source for developing innovative drugs [4,5], currently, natural compounds of interest are under investigation for improving their bioavailability by employing different technologies [6,7].

(*Curcuma longa*) is extensively used as a spice, food preservative and colouring material in India, China and South East Asia. It has been used in traditional medicine as a household remedy for various diseases, including biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism and sinusitis. For the last few decades, extensive work has been done to establish the biological activities and pharmacological actions of turmeric and its extracts. Curcumin (diferuloylmethane), the main yellow bioactive component of turmeric has been shown to have a wide spectrum of biological actions. These include its antiinflammatory, antioxidant, anticarcinogenic, antimutagenic, anticoagulant, antifertility, antidiabetic, antibacterial, antifungal, antiprotozoal, antiviral, antifibrotic, antivenom, antiulcer, hypotensive and hypocholesteremic activities [8, 9, 10].

In this context, we have developed an experimental approach that aims to study the antioxidant power of curcumin and its impact on neurobehavioral alterations and complications on the emotional state announced by the (Open Field) behavioral test and complications, besides biochemical parameters of induced- Formaldehyde Wistar rats.

## **Material And Methods**

### **Animals**

The biological material base that we have chosen is the rat *Rattus rattus* of the Wistar strain from Pasteur Institute in Algiers. The rats are nocturnal mammals of the order of rodents. Upon their arrival, the rats weighed an average of 180 grams, and at the time of the experiment, they weighed on average  $250 \pm 20$  grams.

The rats were acclimated under standardized conditions of natural photoperiod, an average temperature of  $22 \pm 4^\circ$  C and humidity of 50-70%. After an adaptation period of three weeks, we have selected 24 males based on weight which we separated into four experimental groups each include six rats (n=6); lot vehicle control CV, lot control treated curcumin CC, lot Formaldehyde vehicle FV, lot treated with formaldehyde and curcumin FC .

## **Treatment of Animals**

### **Administration of Formaldehyde**

Toxicity was induced in rats by intraperitoneal injection of Formaldehyde (Sigma Lowis ST, Mo) at a dose of 10 mg / kg body weight according to Mahmoud and Fenghour 2016 [11] after dilution with distilled water.

### **Administration of curcumin**

Administration is by gastric gavages of rats to a high dose of 60 mg / kg body weight. Treatment with vehicle or the antioxidant olive oil for controls Administration is by gastric gavages of rats to a high dose of 60 mg / kg body weight. Treatment with vehicle or the antioxidant olive oil for controls started on the 8th day after the injection of formaldehyde and its administration was by gastric tube for 7 days.

### **The test of open field (Open Field, OF)**

The OF test, first described by Hall in 1934 [12], the device is a Plexiglas platform (70cm x 70cm x 40cm) divided into central and peripheral area. Each rat was placed individually in the center of the floor for 5 minutes and allowed exploration [13]. An animal considered anxiety will tend to prefer the peripheral zone Parameters measured the time spent in the center, time spent in the periphery and the distance traveled.

### **Determination of ACTH levels in plasma**

This test is realized in plasma on immunometrique sequentiel chimiluminescent phase solid [14].

The solid phase is a covered ball of murinemonoclonal antibody anti ACTH. The liquid phase is the alkaline phosphatase (an enzyme which amplifies the chimiluminescence for the antigen detection) combined with an antibody polyclonal of doe anti ACTH in reagent ACTH.

## **Statistical analysis**

The results were obtained using the XLSTAT 2014 software in the form of histograms and were treated by Student's t-test, which allowed us to compare the results of the groups treated with formaldehyde versus the Controls groups.

## **Results**

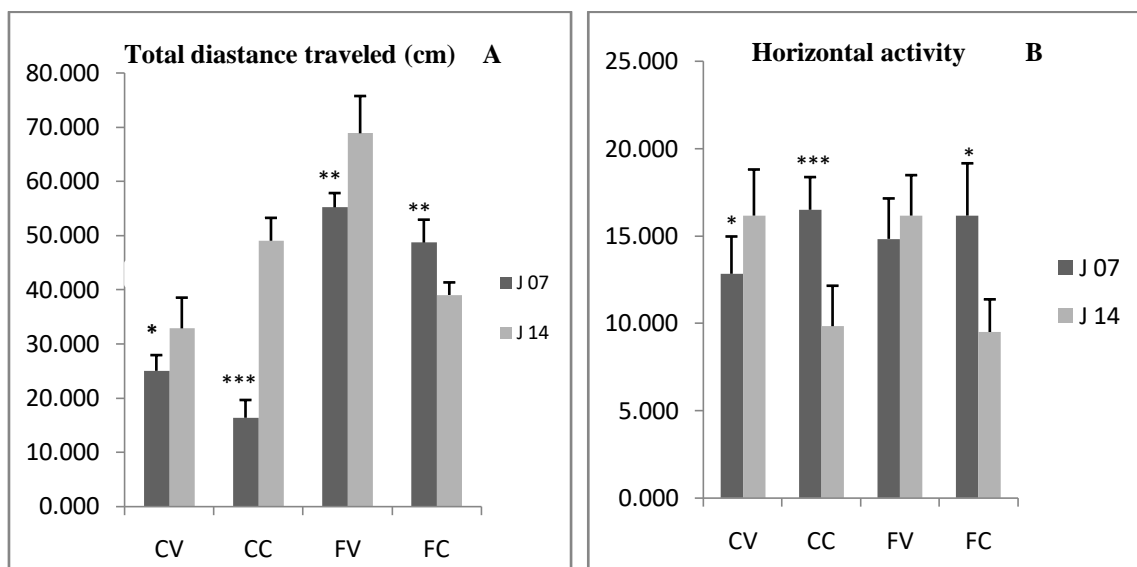
### **Variation of the open Field Test parameters**

The rats were subject to an open field test session on the 7<sup>th</sup> day and second session on the 14<sup>th</sup> day of testing for groups (control and treated).

**Figure A**, The results obtained in this study show a highly significant increase (\*\*\*)  $p < 0,001$ ) of the number of cells crossed by the group control treated with curcumin on the second session (14<sup>th</sup> day) compared to first session (7<sup>th</sup> day).

The distance traveled by the rats treated with olive oil was very significant increase (\*\* $p < 0,01$ ) on the second session compared to the first session.

**Figure B**, the rats were subjected to horizontal activity and statistically analyzed to visualize a highly significant decrease (\*\*\*)  $p < 0,001$ ) at the group control treated with curcumin on the 14<sup>th</sup> day compared to 7<sup>th</sup> day, and a significant decrease ( $p < 0,05$ ) at the group of animals treated with curcumin.



**Figure 1:** Variation of the Open field test parameters (The distance traveled, horizontal activity)

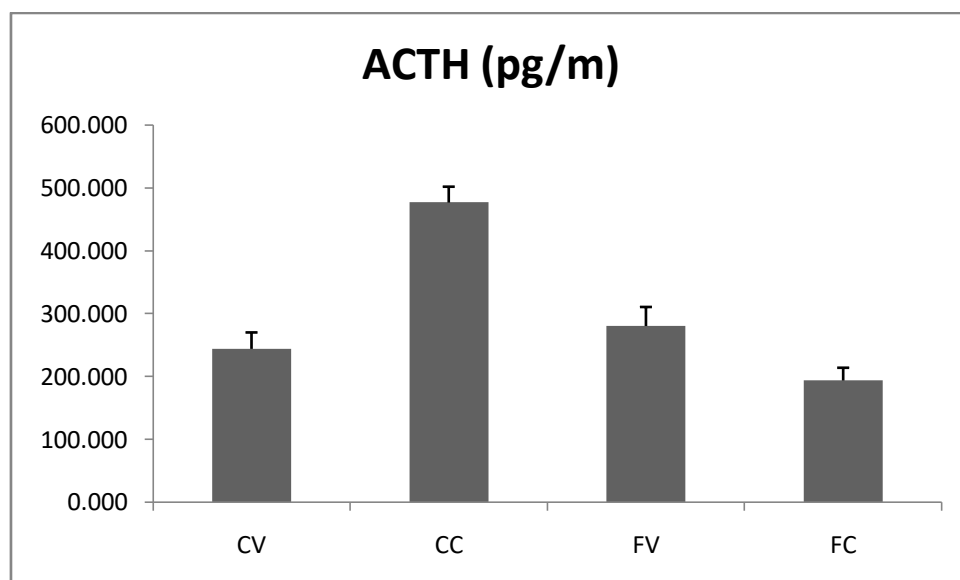
The results are expressed on  $\pm$  SEM (n=6).

Ns. (insignificant difference  $p > 0.05$ ; \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ )

### Variation of ACTH levels

The results obtained in this study shows that the level of ACTH plasmatic in rats treated with formaldehyde was decrease contribution to the controls rats treated with curcumin.

The results showed a increase in level of ACTH plasmatic in controls rats treated with curcumin compared to the group controls vehicle.



**Figure-2:** Variation of ACTH levels in pg /ml The results are expressed on  $\pm$  SEM (n=6).

Ns. (insignificant difference  $p > 0.05$ ; \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ )

## DISCUSSION

Our experimental study is the first of its kind to assess the protective effects of curcumin against formaldehyde-induced neurotoxicity and neurobehavioral in rats.

In this study Toxicity and stress was induced in rats by intraperitoneal injection of Formaldehyde, It has many routes of entry to the body like the dermis, Lino-dos-Santos-Franco et al exposed allergic rats to inhalational formaldehyde and observed increased gene expression and stress [15]. Some studies have demonstrated the link between chronic exposure to AF and the pathological consequences in terms of cancers, teratogenic effects, and neurodegenerative and vascular diseases [16]. Neurotoxicity is defined as a structural change or functional impairment of the nervous system, which originates from exposure to physical, biological, or chemical agents [17] In adults, it often involves peripheral jumpy system effects because the central nervous system (CNS) is well protected by the blood-brain barrier, which prevents the passage of many endogenous and exogenous toxic agents into the brain [18]. The open-field test was used to evaluate the locomotion and rats' exploratory behavior, Our study showed that rats exposed to Formaldehyde had depression, which means a highly significant decrease in test parameters (traversed distance and the horizontal activity). According to Exposure to different FA concentrations in mice affects locomotor activity, depressive and anxious behavior, and cognition like other chemical aggressors [19]. Behavioral studies of animal models are of great importance as they allow the detection of different neurotoxicity forms.

The administration of curcumin to the rats after 7 days in our work mention a hierarchical efficiency of curcumin against different levels of disorders caused by the disease. Our results were in agreement with Lee 2018 [20] examined the effects of curcumin (20, 50, or 100 mg/kg, i.p., once daily) for 14 days after exposure to stress on symptoms of anxiety in rats showed the dysfunction of serotonin (5-HT).

Cortisol or hydrocortisone synthesis is regulated by the pituitary hormone adrenocorticotrophic hormone (ACTH), which is released in response to stimulation by a neuropeptide called corticotrophin-releasing factor produced in the hypothalamus[21], Our results have showed a decrease level of ACTH plasmatic in rat vehicle treated with Formaldehyde contribution to the controls vehicle.

### **Conclusion**

Our results confirm that formaldehyde toxicity induces neurobehavioural disturbances, anxiety and cognitive ability in male rats, the exploitation of the biological potential of plant species is of great interest. Hence, the new approaches consist of looking for active ingredients in natural products of plant origin.

For these reasons, A natural substance that has shown amazing effects for the treatment during the therapy in Wistar rats is Curcumin The behavior of the rats was measured by behavioral tests: the open-field test to measure the level of anxiety. The results show the effectiveness of curcumin in the prevention of behavioral disorders and its ability to improve the damage associated with the administration of formaldehyde.

### **COMPETING INTERESTS**

The authors declare no conflict of interest.

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