

Undesired Effects of Bioinsecticides Molecules in Wistar Rats: Case of Spirotetramat, Citrulus Colocynthis and Cleome Arabica Extracts

BOUBLATA Nour El Iméne

Department of Biology, Faculty of Sciences, University Badji Mokhtar, Annaba 23000, Algeria,
imeneboulata@gmail.com

Manel BEKHAKHECHE

Department of Biology, Faculty of Sciences, University Badji Mokhtar, Annaba 23000, Algeria,
bekhakhechemanel21300@yahoo.fr

Sarra HABBACHI

Department of Biology, Faculty of Sciences, University Badji Mokhtar, Annaba 23000, Algeria,
sarrahabachi@yahoo.com

FatmaZohra SAADANE

Department of Biology, Faculty of Sciences, University Badji Mokhtar, Annaba 23000, Algeria,
saadanezahra2@gmail.com

BOUZAR Abir

Department of Biology, Faculty of Sciences, University Badji Mokhtar, Annaba 23000, Algeria,
bouzarabir2020@yahoo.com

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Cover Page Footnote

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Authors

BOUBLATA Nour El Iméne, Manel BEKHAKHECHE, Sarra HABBACHI, FatmaZohra SAADANE, BOUZAR Abir, HABBACHI Wafa, REBBAS Khellaf, and TAHRAOUI Abedkrim

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UNDESIRE EFFECTS OF BIOINSECTICIDES MOLECULES IN WISTAR RATS: CASE OF SPIROTETRAMAT, *CITRULUS COLOCYNTHIS* AND *CLEOME ARABICA* EXTRACTS

BOUBLATA NOUR EL IMÉNE*¹, BEKHAKHECHE MANEL², HABBACHI SARRA², SAADANE
FATMAZOHRA², BOUZAR ABIR², HABBACHI WAFI², REBBAS KHELLAF^{3,4}, AND TAHRAOUI
ABEDKRIM²

¹ *Laboratory of Environmental Biosurveillance, Department of Biology, Faculty of Sciences,
University Badji Mokhtar, Annaba 23000, Algeria.*

² *Laboratory of Applied Neuroendocrinology, Department of Biology, Faculty of Sciences,
University Badji Mokhtar, Annaba 23000, Algeria.*

³ *Laboratory of Agro-Biotechnology and Nutrition in Arid and Semi-Arid Zones, Ibn Khaldoun -
University, Tiaret, Algeria.*

⁴ *Department of Biology, Faculty of Sciences, University Med Boudiaf, M'Sila 28000, Algeria.*

Corresponding author's email: imeneboubлата@gmail.com

ABSTRACT

The use of pesticides is becoming an indispensable technique in most agricultural practices, regardless of the level of development of the country. Currently, the pesticides used are often less toxic and more specific and are based on insect physiology. Recent studies indicate that pesticide intoxication induces oxidative stress. This work aims to study the neurobehavioral consequences of the administration of two insecticides currently widely used in agriculture: spirotetramat (an inhibitor of lipid synthesis in insects) and the ethanolic extract of *Citrullus colocynthis* (a plant endemic to the Algerian Sahara) and the ethanolic extract of *Cleome arabica* (*Capparidaceae*). The different behavioral tests (elevated cross maze, open fields and forced swimming) show that they have a significant impact on the degree of anxiety of rodents. These products significantly influence the biochemical parameters (blood sugar, cholesterol, triglycerides, urea, creatinine), the hormone Adreno CorticoTropic Hormone, acetylcholine esterase, immune parameters and organ weight.

Keywords: Insecticides, spirotetramat, *Citrullus colocynthis*, *Cleome arabica*, Wistar rat.

Abbreviations: ACTH hormone: Adreno CorticoTropic Hormone, AchE: acetylcholine esterase, EPM: Elevated plus maze, OP: open field, FST: forced swimming test, WBC: White Blood cells, RBC: Red Blood cells, PLT: platelets, HB: Haemoglobin, LYM: Lymphocytes, Mono: Monocytes, MCHC: Mean corpuscular hemoglobin concentration,

INTRODUCTION

Among the most used chemical substances in our environment, pesticides and related products are undoubtedly the most important. The use of these phytopharmaceutical products contributes to take preventive measures against crop pests and to harvest healthy products (Turner et al., 2007). Pesticides are an important issue for the quality of our food and our environment because they have

become an almost indispensable technique in most agricultural practices, whatever the level of the country development. Their use has also contributed to the improvement of public health by controlling certain insect vectors of diseases (Ramade, 2005; Habes et al., 2013; Messiad et al., 2015). With the massive use of pesticides have appeared clear signs of toxicity and adverse effects for the environment and for humans (Eriksson et al., 1990; Eriksson et al., 1992; Snedeker, 2001; Den Hond and

Schoeters, 2006; Bonde et al., 2008). However, due to their massive use, they are nowadays at the heart of an environmental problem, with a contamination of the fauna and flora, as well as a sanitary problem (Snedeker, 2001; Den-Hond and Schoeters, 2006; Schoeters and Hoogenboom, 2006; Bonde et al., 2008). Indeed, due to their toxic properties, pesticides represent a real danger for humans when they are not used under appropriate conditions (Hemingway et al., 1993; Kristensen et al., 2005; Dong et al., 2007; Lee et al., 2007).

Biological control has recently been integrated to control pests. Natural pesticides, resulting from the development of biotechnology, are broadly defined as originating from living organisms: animals, plants, bacteria or certain minerals (Sporleder and Lacey, 2013). Biological control takes many forms, but it is today the natural plant-based products which attract researchers' attention (Boutaleb-Joutei, 2010). Spontaneous plants in drylands are considered as plant genetic resources of agronomic, economic, ecological and strategic interest (UNESCO, 1960). Toxicity studies on pesticides in target and non-target organisms are often restricted to various forms of direct and acute toxicity. Some neurotoxic effects of pesticides are in fact associated with a different kind of organism-development toxicity. This is developmental neurotoxicity, which is therefore related to "environmental exposure" in which some pesticides play a key role. Several studies have shown that gestational or neonatal exposure to pesticides causes neurobehavioral alterations in the offspring at different developmental stages, such as those of Chanda Pope (1996); Lassiter et al., (1998); Levin et al., (2002) and Laura et al., (2004). The purpose of this research is to determine the effectiveness and the neurobehavioral consequences of the administration of three insecticidal molecules: the first is widely used in

agriculture: spirotetramat (a reduced-risk chemical that is an inhibitor of lipid synthesis in insects), the second is the ethanolic extract of *Citrulluscolocynthis* (*Cucurbitaceae*) (commonname hantel, a spontaneous plant of the Algerian Sahara), and the third is the ethanolic extract of *Cleome arabica* (*Capparidaceae*) (commonname: natten, a spontaneous plant of the Algerian Sahara) on Wistar rat (as research model). These insecticidal molecules was administered by ingestion to determine their behavioral effects on rats anxiety and stress, also, we determine their biochemicals and immunities effects.

MATERIAL AND METHODS

i. *Animal*

For all experiments, we used adult rats "*Rattus rattus*" - Wistar strain from the Pasteur Institute (Algiers, Algeria). Rats were raised in sawdust-lined plastic cages with a steel lid and baby bottles filled with water. Rat's food is made in the sticks form consisting of corn, barley, milk and vitamin supplement. These animals were acclimatized to laboratory conditions (temperature 25 ± 2 °C and humidity 70 – 80 % and photoperiod 12:12 h).

ii. *Spirotetramat*

Spirotetramat is a spirocyclic tetramic acid derivative; it's the only foliar insecticide and exclusively developed by Bayer Crop Science. The product has a novel and unique action mode, classified as an inhibitor of acetyl CoA carboxylase or an inhibitor of insect's lipid biosynthesis. Spirotetramat is an oral intoxicant and is active mainly on immature insects (Bell, 2013).

iii. *Citrullus colocynthis* (*Cucurbitaceae*)

It's a spontaneous plant in arid area of Africa and Asia. It's very common in Sahara. Used in traditional medicine to

treat excess sugar, which explain the intoxications frequency in the Maghreb (Hammiche et al., 2013). The toxicity is due to cucurbitacins and their glycosides present throughout the plant, particularly in fruit and seeds (Darwish-Sayed et al., 1974, Seger et al., 2005). The plant used in this study was collected in south central Algeria (Laghouat) (33°48'24" north latitude, 2°52'56" east longitude) and we used the seeds for extraction with ethanol.

iv. *Cleome arabica* (Capparidaceae)

It is a plant with a foul odour, toxic and hallucinogenic effects (Gubb, 1913; Ozenda, 1991). The plant is used in traditional medicine as a diuretic and against rheumatism; it is also a therapeutic and anti-bacterial plant (Ladhariet al., 2013). The effect of this species has also been proven against different orders of insects (Doumandji-Mitiche and Doumandji, 1993; Ozenda, 1991; N'Guessan et al., 2009; Koïta et al., 2012). For the present study, the plant was collected in the Bousaada region (M'sila, Algeria) (33°48'24" north latitude, 2°52'56" east longitude).

v. *Plants extracts*

a. *Preparation of the C. arabica Ethanolic Extract*

Ethanolic maceration follows the Bouharb's et al., protocol (2014). This one consists in macerating 400g of plant powder for 24 hours in one liter of ethanol solvent at (99.8 %) at room temperature and in the shade. After filtration, the solution obtained was evaporated in the shade and with the help of a magnetic stirrer to drive out the solvent (Keita et al., 1998) using a hot plate at a 50 °C temperature until a paste was obtained, which was kept at 4 °C until its use. On each bottle are noted the preparation date, extraction type and concentration. The plant was identified by Pr. RebbasKhellaf,

Department of Biology, Faculty of Science and University of M'sila (Algeria).

b. *Preparation of the C.colocynthis Ethanolic Extract*

We recovered the seeds from the fruit of the plant and dried them at room temperature. They were then processed into a fine powder using an electric grinder. Five hundred grams of the powder were macerated in one liter of absolute ethanol (99.8 %) for 24 hours. After filtration, the filtra was evaporated using a hot plate at a temperature of 50 °C. The recovered paste was stored at 4 °C until use.

v. *Treatments*

To studied indirect effects of Spirotetramat, twenty rats were divided into two groups: a control group (10 individuals: 5 males and 5 females) and a treated group (10 individuals: 5 males and 5 females). These animals have 10 % of spirotetramat (15µg/ml) during 7 days (every other day). For *C. colocynthis*, thirty rats were separated into two groups, a control group (10 individuals: 5 males and 5 females) and a treated group (20 individuals: 10 males and 10 females). These animals have 2ml of *C. colocynthis* (20 µg/ml). One milliliter of *C. arabica* (0.20 µg/l) was administred for 7 days (every other day). All treatments are doing by gavages. The animals were fasted for 8-12 hours before blood collection at the end of the experiment to prevent interfering with the examination of blood glucose and serum lipid profile. Hematological and biochemical characteristics were measured in blood and serum samples, as well as important organ weights.

vi. *Rat's Behaviors in different Anxiety-provoking Situations*

We tested the different rats groups using experimental devices recognized by the scientific society who's most used

elevated plus maze (EPM) (Rodgers and Dalvi, 1997; VanGalen and Steckler, 2000; Karl et al., 2003; Elizalde et al., 2008), and the forced swimming test or Porsolt test (FST) (Porsolt et al., 1977; Karl et al., 2003; Elizalde et al., 2008).

vii. Effect on certain Biochemical Parameters

Blood is collected from control adults, Spirotetramat's adults, *C. colocynthis*'s adults and *C. arabica* 's adults. The separated plasma is frozen and stored immediately at (-20 °C). ACTH plasmas were measured by radioimmunoassay (Raff et al., 2004). We also performed a blood glucose, cholesterol, triglyceride, urea, creatinine and AChE (Acetyl Choline Esterase) assay.

viii. Data Analysis

The various study data were analyzed by descriptive and comparative methods (variances analysis) on XLStat 2009 software. The multivariate analysis (MANOVA) with SPSS Statistics 22.0 enabled us to test treatment and sex effects on the rat behaviors tested and biochemical parameters.

RESULTS

In the elevated plus maze test on results show that the time spent in the center of the device is more important in female rats treated with ethanolic extract of *C. Arabica* 60.67 ± 20.82 seconds compared to the other groups (Tab.1). It is also found that female rats treated with ethanolic extract of *C. colocynthis* spend less time in the center of the device which is 9.08 ± 5.55 seconds compared to the other groups (Tab.1). The multivariate test by a GLM on SPSS-22 shows that the time in the center is mainly a function of the treatment. Table 1 shows that sex does not influence the time spent in the center of control and treated rats ($p: 0.99$). The

multivariate analysis indicates a very highly significant effect of the treatment with the *C. arabica* plant on the time spent in the center ($p: 0.000$) (Tab. 1); we recorded no effect of the sex-treatment intersection on the time spent in the center of the studied rats ($p: 0.05$) (Tab.1). We recorded that the time spent in the open arms of the maze increased in male rats treated with the ethanolic extract of the *C.arabica* plant 61.87 ± 1.35 seconds (Tab.1) while this time decreased in female rats treated with this plant 3.57 ± 0.42 seconds (Tab.1). Table 1 show that gender has a very highly significant effect on the time spent in the open arm of control and treated rats ($p: 0.000$). The multivariate analysis indicates a highly significant effect of the treatment with *C. arabica* plant on the time spent in the open arms ($p: 0.000$) (Tab. 1); we recorded no effect of the sex-treatment intersection on the time spent in the open arms of the studied rats ($p: 0.05$) (Tab. 1). In males treated with ethanolic extract of the *C.arabica* plant, the time spent in the closed arms decreased compared to the other groups and was 195.26 ± 37.10 seconds (Tab.1) while in females treated with ethanolic extract the time spent in the closed arms increased compared to the controls and we recorded an average of 296.96 ± 0.38 seconds in this group of animals (Tab.1). Table 1 showed that gender has a highly significant effect on the time spent in the closed arm of control and treated rats ($p: 0.000$). The multivariate analysis indicates a highly significant effect of the treatment with *C. arabica* plant on the time spent in the closed arms ($p: 0.001$) (Tab. 1); we also recorded a highly significant effect of the intersection of sex and treatment on the time spent in the closed arms of the rats studied ($p: 0.000$) (Tab.1). In terms of the number of entries in the open arms, females treated with with ethanolic extract of *C. arabica* showed an increase in this number, which was 3.00 ± 0.40 entries, and a decrease in this number in the

females treated with ethanolic extract of *C. colocynthis*, which was 0.70 ± 1.06 entries. Sex had a significant effect on the number of entries in the open arm of control and treated rats ($p: 0.03$). The multivariate analysis indicates a significant effect of the treatment with *C. arabica* plant on the number spent in the open arms ($p: 0.01$) (Tab. 1); we recorded a significant effect of the sex-treatment intersection on the number of entries in the open arms of the studied rats ($p: 0.01$) (Tab.1). The number of entries in the closed arms was increased in the females treated with ethanolic extract of *C. arabica* to 6.25 ± 0.75 entries and decreased in the females treated with ethanolic extract of *C. colocynthis* to 1.7 ± 0.95 entries. Sex had no significant effect on the number of entries in the closed arm of control and treated rats ($p: 0.29$). Multivariate analysis indicated a significant effect of treatment with *C. arabica* plant on the number of entries in the closed arms ($p: 0.01$) (Tab.1); we recorded no effect of the sex-treatment intersection on the number of entries in the closed arms of the rats studied ($p: 0.11$) (Tab.1). In the females treated with Spirotetramat, the number of straightenings increased compared to the controls and was 18.40 ± 8.88 straightenings (Tab.1), whereas in the males treated with ethanolic extract *C.arabica*, the number of straightenings decreased compared to the controls and we recorded an average of 8.00 ± 1.03 straightenings (Tab.1). The multivariate test by a GLM on SPSS-22 shows that the number of turnarounds is mostly a function of treatment. Table 1 showed that gender had no effect on the number of turnarounds in control and treated rats ($p: 0.06$). Multivariate analysis indicates a highly significant effect of treatment on the number of turn arounds ($p: 0.003$) (Tab. 1); we recorded a very highly significant effect of the sex-treatment

intersection on the number of turnarounds of the rats studied ($p: 0.000$) (Tab.1).

In the forced swimming test, the swimming time in the control females was an average of 147.20 ± 5.69 (Tab.2) seconds, but this time decreased to an average of 28.40 ± 19.29 (Tab.2) seconds in the females treated with the ethanolic extract of *C. colocynthis*. Table 3 shows that sex has no effect highly on the swimming time of control and treated rats ($p: 0.29$). The multivariate analysis indicates the very highly significant effect of the treatment with the *C. colocynthis* plant on the swimming time ($p: 0.000$) (Tab. 2); we also recorded, no significant effect of the sex-treatment intersection on the swimming time of the studied rats ($p: 0.57$) (Tab. 2). In females treated with spirotetramat, the immobility time decreased compared to controls and was 63.00 ± 39.95 seconds (Tab.2), we also recorded that this time increased in males treated with aqueous extract of *C.arabica* and was 172.86 ± 16.60 seconds (Tab.2). Sex has a very highly significant effect on the immobility time of control and treated rats ($p: 0.000$). The multivariate analysis indicates a highly significant effect of the treatment with the plant on the immobility time ($p: 0.000$) (Tab. 2); we also recorded a highly significant effect of the intersection of sex and treatment on the immobility time of the rats studied ($p: 0.002$) (Tab.2). In females treated with the extract ethanolic of the *C.arabica* plant, the climbing time decreases compared to controls and is 0.98 ± 0.26 seconds (Tab.2) whereas in females treated with spirotetramat climbing time increases compared to controls and we recorded an average of 174.00 ± 66.42 seconds in this group of animals (Tab.2). The multivariate test by a GLM on SPSS-22 shows that the climbing time is mainly a function of the treatment. Table 3 shows that gender has no effect on the climbing time of control and treated rats ($p: 0.10$).

Table 1: Effect on rat's behavior (in plus maze).

	♂				♀				Treatment	Sex	Treatment * sex
	Moy ± SEM				Moy ± SEM						
	C	Sp	Cc	Ca	C	Sp	Cc	Ca			
Time spent in center (s)	33.20 ± 17.64	19.60 ± 11.48	21.59 ± 11.12	56.69 ± 20.31	11.00 ± 7.31	45.00 ± 27.15	9.8 ± 5.55	60.67 ± 20.82	0.000***	0.99	0.05
Time spent in open arms (s)	18 ± 24.22	11 ± 8.94	22.58 ± 26.04	61.87 ± 1.35	25.80 ± 23.00	15.20 ± 11.43	14.80 ± 21.85	3.57 ± 0.42	0.000***	0.000***	0.05
Time spent in closed arms (s)	243.20 ± 12.46	269 ± 14.10	255.50 ± 24.05	195.26 ± 37.10	257 ± 24.40	242.80 ± 26.64	275.40 ± 26.71	296.96 ± 0.38	0.000***	0.001**	0.000***
Number of open arms	0.80 ± 0.84	0.80 ± 0.84	1.21 ± 1.06	2.75 ± 0.75	2 ± 1.58	1.40 ± 1.14	0.7 ± 1.06	3.00 ± 0.40	0.01*	0.03*	0.01*
Number of closed arms	5.40 ± 2.70	3.80 ± 1.30	2.93 ± 1.29	4.25 ± 0.25	2.80 ± 1.48	4 ± 1.87	1.7 ± 0.95	6.25 ± 0.75	0.01*	0.29	0.11
Number of redress	11 ± 1.58	14.20 ± 5.44	17.49 ± 7.82	8.00 ± 1.03	11.40 ± 3.85	18.40 ± 8.88	8.5 ± 3.81	8.16 ± 2.44	0.003**	0.06	0.000***

[Mean: Mean; SEM: Standard deviation of the mean; C: Control; ♂: Male; ♀: female; ♀; Ca: *C. arabica*; Sp: *spirotetramat*; Cc: *C. colocynthis*] [* significant*; ** highly significant; *** very highly significant]

Table 2: Effect on rat's on depressive state.

	♂				♀				Treatment	Sex	Treatment * sex
	Moy ± SEM				Moy ± SEM						
	C	Sp	Cc	Ca	C	Sp	Cc	Ca			
Swimming time (s)	111.20 ± 28.68	66.40 ± 52.88	35.1 ± 24.24	131.15 ± 18.44	147.20 ± 50.96	43 ± 36.17	28.40 ± 19.29	101.12 ± 13.70	0.000***	0.29	0.57
Climbing time (s)	60.20 ± 22.29	158.80 ± 63.43	46 ± 43.90	1.38 ± 0.29	40.80 ± 29.68	174 ± 66.42	105 ± 37.57	0.98 ± 0.26	0.000***	0.10	0.31
Time of immobility (s)	122.40 ± 29.01	74.60 ± 29.46	74.60 ± 13.17	172.56 ± 16.60	103 ± 34.48	63 ± 39.95	63.20 ± 17.87	191.45 ± 13.42	0.000***	0.000***	0.002**

[Mean: Mean; SEM: Standard deviation of the mean; C: Control; ♂: Male; ♀: female; ♀; Ca: *C. arabica*; Sp: *spirotetramat*; Cc: *C. colocynthis*] [* significant*; ** highly significant; *** very highly significant]

Table 3: Effect on various biochemical parameters, ACTH hormone and AChE

	♂				♀				Treatment <i>p</i>	Sex <i>p</i>	Treatment * sex <i>p</i>
	Moy ± SEM		Moy ± SEM		Moy ± SEM		Moy ± SEM				
	C	Sp	Cc	Ca	C	Sp	Cc	Ca			
Glycemia (g/l)	1.02 ± 0.38	0.95 ± 0.14	1.17 ± 0.23	0.61 ± 0.04	0.82 ± 0.10	0.98 ± 0.18	1.10 ± 0.15	0.65 ± 0.01	0.0001***	0.48	0.77
Urea (g/l)	0.52 ± 0.16	0.69 ± 0.06	0.60 ± 0.12	0.25 ± 0.01	0.35 ± 0.05	0.49 ± 0.04	0.62 ± 0.15	0.25 ± 0.02	0.000***	0.04*	0.11
Creatinine (mg/l)	3.86 ± 0.66	4.95 ± 0.25	5.06 ± 0.34	7.12 ± 0.09	3.41 ± 0.56	4.99 ± 0.70	6.72 ± 0.47	7.43 ± 0.14	0.000***	0.05	0.000***
Triglyceride (g/l)	0.75 ± 0.15	0.61 ± 0.03	0.49 ± 0.15	0.54 ± 0.03	1.12 ± 0.25	0.62 ± 0.27	0.55 ± 0.30	0.60 ± 0.07	0.02*	0.44	0.56
Cholesterol (g/l)	0.45 ± 0.10	0.38 ± 0.09	0.61 ± 0.15	0.93 ± 0.02	0.43 ± 0.11	0.38 ± 0.09	0.56 ± 0.08	0.33 ± 0.10	0.000***	0.005**	0.001**
ACTH (pg/ml)	89.19 ± 31.40	14.47 ± 18.07	536.80 ± 137.99	6.02 ± 1.33	100.08 ± 29.93	19.24 ± 16.72	22.69 ± 30.58	9.13 ± 3.53	0.000***	0.000***	0.000***
AChE (nml/min/mg Protein)	0.16 ± 0.03	0.13 ± 0.05	0.06 ± 0.02	0.09 ± 0.03	0.19 ± 0.03	0.13 ± 0.03	0.09 ± 0.02	0.02 ± 0.00	0.000***	0.34	0.74

[Mean: Mean; SEM: Standard deviation of the mean; C: Control; ♂: Male; ♀: female; ♀: ♀; Ca: *C. arabica*; Sp: *spirotetramat*; Cc: *C. colocynthis*] [* significant*; ** highly significant; *** very highly significant]

Multivariate analysis indicates a very highly significant effect of treatment on climbing time ($p: 0.000$) (Tab.2); we also recorded no effect of the sex-treatment intersection on the climbing time of the studied rats ($p: 0.31$) (Tab.2).

Concerning the biochemical parameters, our results showed that the blood sugar level in rats treated with ethanolic extract of *C.arabica* decreased and is 0.65 ± 0.01 g/l (Tab.3), on the other hand this level increased in males treated with ethanolic extract of the *C.colocynthis* plant and is 1.17 ± 0.23 g/l (Tab.3). Sex did not influence the blood glucose level of control and treated rats ($p: 0.48$). The multivariate analysis indicated the significant effect of the treatment with the plant on the blood glucose level ($p: 0.001$) (Tab. 3); we recorded no effect of the sex-treatment intersection on the blood glucose level of the studied rats ($p: 0.77$) (Tab. 3). The spirotetramat induced an increase in the urea level in the treated male rats and is 0.69 ± 0.06 g/l (Tab.3) compared to the other groups. The plant *C.arabica* decreased this level in the treated animals in both sexes and is 0.25 ± 0.01 g/l in males and is 0.25 ± 0.02 g/l in females (Tab.3). Sex significantly influenced the urea level of control and treated rats ($p: 0.04$). The multivariate analysis also showed a highly significant effect of the treatment with urea on the urea level ($p: 0.000$) (Tab. 3); we also recorded no effect of the intersection of sex and treatment on the urea level of the rats studied ($p: 0.11$) (Tab. 3). In females treated with ethanolic extract of *C. arabica*, the creatinine level increased in comparison with the males treated with ethanolic extract of *C. arabica* other groups and is 7.43 ± 0.14 mg/l (Tab.3). The multivariate test by a GLM on SPSS-22 shows that creatinine is mainly a function of the sex of the studied animal. Table 4 shows that sex has no effect on the creatinine level of control and treated rats ($p: 0.05$). The multivariate analysis also indicates that the nature of the extract used has a highly significant

effect on the creatinine level ($p: 0.000$) (Tab. 3); we recorded a highly significant effect of the sex-treatment intersection on the creatinine level of the rats studied ($p: 0.000$) (Tab. 3). It is noted that the average triglyceride level decreased after treatment with ethanolic extract *C. colocynthis* in males and females by 0.49 ± 0.15 g/l compared to controls (Tab.3). Sex did not influence triglyceride levels in control and treated rats ($p: 0.44$). Multivariate analysis indicated that treatment had a significant effect on triglyceride levels ($p: 0.02$) (Tab. 3); we recorded no effect of the sex-treatment intersection on triglyceride levels in the rats studied ($p: 0.56$) (Tab. 3). In the females treated with the ethanolic extract of the Saharan plant *C.arabica*, the average cholesterol level decreased after the treatment compared to the controls and was 0.33 ± 0.10 g/l (Tab.3) On the other hand this level is high in males treated with the ethanolic extract of the *C. colocynthis* plant and is 0.61 ± 0.15 g/l (Tab.3). Sex has a highly significant effect on the cholesterol level of control and treated rats ($p: 0.005$). The statistical study also shows that there is a highly significant effect of the nature of the treatment with the *C. arabica* plant on the cholesterol level ($p: 0.000$) (Tab. 3); we recorded, also, that the two parameters sex and treatment act in intersection (sex-treatment) on the cholesterol level, we recorded a highly significant effect of on the cholesterol level of the studied rats ($p: 0.001$) (Tab. 3). For the effect on stress hormone, our results show that *C.arabica* diminishes the level of ACTH hormone in males and is 6.02 ± 1.33 pg/ml (Tab.3) but *C.colocynthis* plant increases the level in male rats and is 536.80 ± 137.99 pg/ml (Tab.3). Sex has a highly significant effect on the level of ACTH hormone in control and treated rats ($p: 0.000$). The statistical study also shows that there is a very highly significant effect of the nature of the treatment on the level of this hormone ($p: 0.000$) (Tab. 3); we recorded, also, that the two parameters sex and treatment act in

intersection (sex-treatment) on the level of the ACTH hormone, we recorded a highly significant effect of on this tax of the studied rats ($p: 0.000$) (Tab. 3). Our results show that there is a highly significant decrease of cholinesterase activity in rats treated with ethanolic extract of *C.arabica* plant in females is 0.06 ± 0.02 nml/min/mg Protein (Tab.3). Sex does not influence the cholinesterase activity of control and treated rats ($p: 0.34$). Multivariate analysis indicated a very highly significant effect of treatment on this activity ($p: 0.000$) (Tab. 3); we recorded no effect of the sex-treatment intersection on the cholinesterase activity of the studied rats ($p: 0.74$) (Tab. 3).

The analysis of immune parameters shows that the number of white blood cells decreases in female rats treated with spirotetramat is 3.77 ± 0.83 μ l (Tab.4) but increases in male rats treated with ethanolic extract of *C. colocynthis* and is 7.66 ± 1.31 μ l (Tab.4). The multivariate analysis indicates that there is a highly significant effect of sex on the white blood cell count of the rats studied ($p: 0.008$). The statistical study also shows that there is no effect of the nature of the treatment on the number of white blood cells ($p: 0.08$) (Tab. 4); we recorded, also, no effect of the intersection of sex-treatment on the number of white blood cells of the studied rats ($p: 0.58$) (Tab.4).The number of red blood cells decreases in the females treated with the ethanolic extract of *C. colocynthis* is 5.40 ± 2.14 μ l (Tab.4) The multivariate analysis indicates that there is no effect of sex on the red blood cell count of the studied rats ($p: 0.23$). The statistical study also shows that there is no effect of the nature of the treatment on the number of red blood cells ($p: 0.83$) (Tab. 4); we also recorded no effect of the intersection of sex and treatment on the number of red blood cells of the rats studied ($p: 0.72$) (Tab.4). The treatment also acts on the level of hemoglobin concentration by an increase in the animals treated with ethanolic extract of *C. arabica* and is

16.86 ± 64 g/dL (Tab.5) and by a decrease of this concentration in the rats treated with spirotetramat and is 11.32 ± 0.61 g/dL (Tab.4) The multivariate analysis indicates that there is no effect of sex on the hemoglobin concentration of the rats studied ($p: 0.05$). The statistical study also shows that there is a highly significant effect of the nature of the treatment on this concentration ($p: 0.001$) (Tab. 4); we also recorded no effect of the sex-treatment intersection on the hemoglobin concentration of the rats studied ($p: 0.27$) (Tab.4). The results obtained show that the average blood volume level increases in the the mean corpuscular volume of animals treated with spirotetramat was 76.08 ± 10.33 fL (Tab.4), whereas the mean corpuscular volume of animals treated with *C. arabica* was 51.05 ± 0.30 fL (Tab.4). The multivariate analysis indicates that there is no effect of sex on the mean corpuscular volume of the rats studied ($p: 0.53$). The statistical study also shows that there is a highly significant effect of the nature of the treatment on the rate of the mean corpuscular volume ($p: 0.000$) (Tab. 4); we also recorded no effect of the intersection of sex and treatment on the rate of the mean corpuscular volume of the rats studied ($p: 0.34$) (Tab.4). In female rats treated with *C. arabica* plant, the rate of the average corpuscular content of hemoglobin increases in comparison with the other groups and is 22.45 ± 0.19 pg (Tab.4). The multivariate analysis indicates that there is a significant effect of sex on the mean corpuscular hemoglobin content of the rats studied ($p: 0.03$). The statistical study also shows that there is a highly significant effect of the nature of the treatment on the average corpuscular hemoglobin content ($p: 0.000$) (Tab. 4); we also recorded a significant effect of the intersection of sex and treatment on the average corpuscular hemoglobin content of the rats studied ($p: 0.02$) (Tab.4). The average corpuscular concentration of hemoglobin increases in animals treated with the *C. arabica* plant in both sexes and

is 40.35 ± 0.35 g/dL in males and 40.21 ± 0.26 g/dL (Tab.4).The multivariate analysis indicates that there is a significant effect of sex on the rate of the average corpuscular concentration of hemoglobin in the rats studied (p : 0.04). The statistical study also shows that there is a highly significant effect of the nature of the treatment on the level of the average corpuscular concentration of hemoglobin (p : 0.000) (Tab. 4); we also recorded a highly significant effect of the intersection of sex and treatment on the level of the average corpuscular concentration of hemoglobin (p : 0.004) (Tab.4). The number of platelets increased in animals treated with *C. arabica* plant in both sexes and was 808.50 ± 100.14 µl in males and 808.33 ± 51.35 µl(Tab.4).The multivariate analysis indicates that there is a highly significant effect of sex on the number of platelets of the studied rats (p :0.008). The statistical study also shows that there is a highly significant effect of the nature of the treatment on the number of platelets (p : 0.000) (Tab. 4); we also recorded a highly significant effect of the intersection of sex and treatment on the number of platelets of the rats studied (p : 0.000) (Tab.4). It was noted that the number of lymphocytes increased after treatment with the ethanolic extract of the *C. colocynthis* plant in females and was 58.17 ± 17.12 µl (Tab.4). The statistical study also shows that there is a highly significant effect of the nature of the treatment on the number of lymphocytes (p : 0.000) (Tab. 4); we also recorded a significant effect of the intersection of sex and treatment on the number of lymphocytes in the rats studied (p : 0.03) (Tab.4). The number of monocytes increased in the females treated with ethanolic extract *C. colocynthis* and was 11.60 ± 4.71 µl (Tab.4), while the number of monocytes decreased in the females treated with spirotetramat and was 0.14 ± 0.07 µl (Tab.4). The multivariate analysis indicated that there was a highly

significant effect of sex on the number of monocytes in the rats studied (p : 0.004). The statistical study also shows that there is a highly significant effect of the nature of the treatment on the number of monocytes (p : 0.000) (Tab. 4); we also recorded a highly significant effect of the intersection of sex and treatment on the number of monocytes of the rats studied (p : 0.000) (Tab.4).

For organ weights, we recorded that the average kidney weight decreased in females treated with *C. arabica* extra-ethanolic and was 0.39 ± 0.01 g (Tab. 5).Table 5 shows that sex had no effect on kidney weights of control and treated rats (p : 0.22). Multivariate analysis indicates a very highly significant effect of treatment with *C. arabica* plant on kidney weight (p : 0.001) (Tab.5); we recorded no effect of the sex-treatment intersection on kidney weight of the studied rats (p : 0.69) (Tab.5). *C.arabica* plant decreased the weight of adrenal glands in animals for both sexes and is 0.01 ± 0.000 g in males and is 0.02 ± 0.001 g in females (Tab.5).Multivariate analysis indicates that there is a highly significant effect of sex on the weight of adrenal glands of the studied rats (p : 0.000). The statistical study also shows that there is a very highly significant effect of the nature of the treatment on the rate of the mean corpuscle volume (p : 0.000) (Tab. 5); we also recorded a very highly significant effect of the intersection of sex and treatment on the weight of the adrenal glands of the rats studied (p : 0.000) (Tab.5). In animals treated with the plant *C.arabica* we found that the weight of the liver decreases after treatment with this plant in both sexes 5.33 ± 0.08 g in males and is 5.50 ± 0.14 g in females (Tab.5).The multivariate test by a GLM on SPSS-22 shows that the time in the center is mainly a function of the treatment. Table 5 shows that sex has a very highly significant effect on liver weight in control and treated rats (p : 0.000).

Table 4: Effect on immune parameters.

	♂				♀				Treatment	Sex	Treatment * sex
	Moy ± SEM		Moy ± SEM		Moy ± SEM		Moy ± SEM		<i>p</i>	<i>p</i>	<i>p</i>
	C	Sp	Cc	Ca	C	Sp	Cc	Ca			
WBC ($10^3/\mu\text{L}\mu\text{l}$)	4.62 ± 0.88	7.11 ± 2.46	7.66 ± 1.31	7.13 ± 0.52	3.89 ± 0.50	3.77 ± 0.83	4.64 ± 3.73	7.03 ± 0.35	0.08	0.008**	0.58
RBC ($\times 10^6/\mu\text{L}\mu\text{l}$)	15.31 ± 19.74	6.71 ± 0.62	8.43 ± 0.54	8.35 ± 0.33	5.50 ± 0.78	6.67 ± 0.83	5.40 ± 2.14	6.79 ± 0.09	0.83	0.23	0.72
HB (g/dL)	10.64 ± 1.20	11.88 ± 0.79	16.44 ± 0.71	16.86 ± 0.64	10.55 ± 1.63	11.32 ± 0.61	12.10 ± 5.43	14.35 ± 0.60	0.001**	0.05	0.27
PVC (fL)	75.70 ± 5.67	71.10 ± 1.48	60.19 ± 1.81	51.05 ± 0.30	72.70 ± 4.10	76.08 ± 10.33	58.49 ± 2.13	55.58 ± 0.82	0.000***	0.53	0.34
TCMH (pg)	17.24 ± 1.01	17.74 ± 0.89	19.53 ± 0.88	20.33 ± 0.22	19.15 ± 0.21	17.06 ± 1.08	21.99 ± 2.11	22.45 ± 0.19	0.000***	0.03	0.02
MCHC (g/dL)	22.94 ± 2.93	24.94 ± 0.95	32.46 ± 1.49	40.35 ± 0.35	24.40 ± 1.84	22.66 ± 2.16	37.55 ± 2.60	40.21 ± 0.26	0.000***	0.04	0.004
PLT ($\times 10^3/\mu\text{L}\mu\text{l}$)	475.60 ± 58.80	325.80 ± 77.42	694 ± 58.35	808.50 ± 100.14	451 ± 62.93	471.60 ± 78.46	275.2 ± 166.67	808.33 ± 51.35	0.000***	0.008**	0.000****
LYM ($\times 10^3/\mu\text{L}\mu\text{l}$)	3.72 ± 0.94	4.29 ± 1.39	16.9 ± 37.79	4.28 ± 0.90	2.89 ± 0.42	2.57 ± 0.40	58.54 ± 17.12	4.91 ± 0.48	0.000***	0.12	0.03*
Mono ($\times 10^3/\mu\text{L}\mu\text{l}$)	0.28 ± 0.11	0.56 ± 0.36	0.98 ± 2.19	1.03 ± 0.06	0.29 ± 0.07	0.14 ± 0.07	11.60 ± 4.71	0.85 ± 0.10	0.000***	0.004**	0.000***

[Mean: Mean; SEM: Standard deviation of the mean; C: Control; ♂: Male; ♀: female; ♀: Ca: *C. arabica*; Sp: *spirotetramat*; Cc: *C. colocynthis*] [* significant*; ** highly significant; *** very highly significant]

Table 5: Effect on organ's weight

	♂ Moy ± SEM				♀ Moy ± SEM				Treatment	Sex	Treatment * sex
	C	Sp	Cc	Ca	C	Sp	Cc	Ca	<i>p</i>	<i>p</i>	<i>p</i>
Brain (g)	1.25 ± 0.24	1.14 ± 0.14	1.17 ± 0.17	1.22 ± 0.04	1.05 ± 0.10	1.16 ± 0.09	1.07 ± 0.33	1.22 ± 0.02	0.84	0.23	0.47
Kidneys (g)	1.06 ± 0.55	1.18 ± 0.15	1.50 ± 0.09	0.43 ± 0.00	1.00 ± 0.07	0.94 ± 0.41	1.24 ± 0.36	0.39 ± 0.01	0.000***	0.22	0.69
The adrenal glands (g)	0.06 ± 0.02	0.05 ± 0.01	0.06 ± 0.01	0.01 ± 0.000	0.05 ± 0.01	0.07 ± 0.0001	0.07 ± 0.02	0.02 ± 0.001	0.000***	0.000***	0.000***
Liver (g)	7.33 ± 1.15	6.02 ± 0.65	7.79 ± 1.90	5.33 ± 0.08	6.02 ± 0.65	6.10 ± 0.85	5.01 ± 0.55	5.50 ± 0.14	0.000***	0.000***	0.000***
Lungs (g)	0.89 ± 0.23	0.94 ± 0.17	1.37 ± 0.26	1.48 ± 0.07	0.88 ± 0.12	0.77 ± 0.77	1.28 ± 0.26	1.42 ± 0.05	0.000***	0.16	0.66

[Mean: Mean; SEM: Standard deviation of the mean; C: Control; ♂: Male; ♀: female; ♀: Ca: *C. arabica*; Sp: *spirotetramat*; Cc: *C. colocynthis*] [* significant*; ** highly significant; *** very highly significant]

Table 6: Treatment effect on rat's anxiety

Effet	Valeur	F	ddl de l'hypothèse	Erreur ddl	p	
Constante	Trace de Pillai	1.000	8379,715 ^b	24.00	1.00	0.00**
	Lambda de Wilks	0.00	8379,715 ^b	24.00	1.00	0.00**
	Trace de Hotelling	201113.172	8379,715 ^b	24.00	1.00	0.00**
	Plus grande racine de Roy	201113.172	8379,715 ^b	24.00	1.00	0.00**
Sexe	Trace de Pillai	0.99	9,704 ^b	24.00	1.00	.249
	Lambda de Wilks	0.00	9,704 ^b	24.00	1.00	.249
	Trace de Hotelling	232.90	9,704 ^b	24.00	1.00	.249
	Plus grande racine de Roy	232.90	9,704 ^b	24.00	1.00	.249
Traitement	Trace de Pillai	2.97	17.206	72.00	9.00	0.00**
	Lambda de Wilks	0.00	19.891	72.00	3.85	0.00**
	Trace de Hotelling			72.00		
	Plus grande racine de Roy	3279.82	409,978 ^c	24.00	3.00	0.00**
sexe * Traitement	Trace de Pillai	2.98	18.546	72.00	9.00	0.00**
	Lambda de Wilks	0.00	23.596	72.00	3.85	0.00**
	Trace de Hotelling	-	-	72.00	-	-
	Plus grande racine de Roy	7446.75	930,844 ^c	24.00	3.00	0.00**

The multivariate analysis indicates a very highly significant effect of the treatment with *C. arabica* plant on the liver mean (p : 0.000) (Tab. 5); we recorded a very highly significant effect of the sex-treatment intersection on the time spent in the center of the studied rats (p : 0.000) (Tab.5).

Spirotetramat decreased the average lung weight in treated females compared to the other groups and is $0.77 \pm 0.77g$ (Tab.5). Multivariate analysis indicates that treatment has a very highly significant effect on the average lung weight of the studied rats (p : 0.000) (Tab.5)

DISCUSSION

The practice of intensive agriculture requires a significant use of phytosanitary products commonly called pesticides. These substances are used to control mainly organisms considered as pests: insects (insecticides), fungi, molds (fungicides), weeds (herbicides), rodents (raticides) (Faki et al., 2019). However, these plant safety products can lead to manifest unforeseen consequences; toxicity in non-target creatures such as useful insecticides; pollution of bodies of water (Kennedy et al., 2012); proved hazardous to humans (Al-Habori et al., 2002; Meeker et al., 2006). The use of chemicals in crop pest management is a necessity. Yet, the negative effects they have on non-target creatures have dubious application (Maxim et al., 2007). Pesticides have harmful effects on humans but also on animals and plants. For example, 15-20% of these products are carcinogenic and most of them are endocrine disruptors (Meyer et al., 2003). In order to control pest populations and limit their proliferation, humans are making considerable efforts and searching for new physical, chemical and biological control methods (Kim et al., 1995, Lyon, 1997). Plant extracts have received a lot of interest in recent years as an alternative to

synthetic pesticides. Against insects, plants have developed a variety of chemical defensive systems (Wink 1993). Plants produce secondary metabolites due to insect interactions (Regnault-Roger et al., 2004; Isman, 2006; Howe and Jander, 2008). These metabolites protect plants against insect pests and might be used in integrated pest management (Schmutterer 1992). The majority of botanical pesticides on the market rely on the effects of plant metabolites that are immediately or chronically poisonous to insects (Dayan et al., 2009; Pavela et al., 2009). Some Capparidacea species have remarkable biological effects, including antibacterial (Mali 2010), anti-diabetic (Yaniv et al., 1987), analgesic, immunomodulatory (Mali 2010), and anti-inflammatory (Al-Saidet et al., 1988; Rossi et al., 1988), antioxidant (Germano et al., 2002), genotoxic (Sultan and Çelik, 2009), anti-allergic, anti-histaminic (Trombetta et al., 2005), antifungal (Ali-Shtayeh and Abu-Ghdeib 1999), antihepatotoxic (Gadgoli and Mishra 1999; Aghel et al., 2007; Mali 2010), and hypolipidemic (Eddouks et al., 2005). Yang and Tang (1988) examined plants used to control insect pests and discovered a tight link between medicinal and pesticidal species, indicating that *C. arabica* may also have insecticidal action.

The active ingredients of plants have now become essential components of our medicines and health care products (Hans, 2007). However, despite the harmlessness of some plants, many species are poisonous in treating numerous disorders, including foxglove, belladonna and colchicum. Indeed, the unconsidered use of medicinal plants can cause serious and sometimes fatal intoxications (Fouché et al., 2000).

In recent years, researchers are interested in in-depth studies and analyses of the therapeutic efficacy as well as the toxicological aspect of plants (De Smet, 1993). For decades, in Algeria, a number of current projects have started development by the use of natural goods,

notably aqueous or ethanol plant extracts, as form of insect control (Aouinty et al., 2006; Kemassi and Oueld El-hadj, 2008; Lbouz, 2010; Kemassi et al., 2012; Habbachi et al., 2013; Kemassi et al., 2014; Merabti et al., 2015; Benhissen, 2016; Merabti, 2016; Masna, 2016; Korichi-Almi et al., 2016; Almi et al., 2016; Benhissen et al., 2018; Bekhakheche et al., 2018; Habbachi et al., 2019; Seglab et al., 2019; Habbachi et al., 2020; Boublata et al., 2020; Saadane et al., 2021).

In this study, we used ethanolic extracts of *C. arabica* and *C. colocynthis* to identify the toxic substances of these plants, in addition to its medicinal capabilities, can be used as a bio-insecticide to limit the proliferation of insect pests.

The elevated plus labyrinth test is based on the conclusion that rats and mice naturally dislike unknown broad areas and are afraid of being balanced on a relatively small raised platform, which might create anxiety among humans (Walf and Trye, 2007); As a result, avoiding open arms is viewed as anxiety-inducing conduct (Crawly and Goodwin, 1980; Belzung and Griebel, 2001). An anxiolytic agent increases exploration of open arms (time and entries in open arms). Diazepam confirmed its anxiolytic effects (Crawly and Goodwin, 1980). The results of this study show that the animals treated with the *C.arabica* plant increased the time spent in open arms compared to the other groups, indicating an anxiolytic type effect, in addition to the fact that this reduction a similar behavior anxiety was similar to that observed after conventional treatment with diazepam. These results are similar to those of (Doukkali et al., 2016; Boublata et al., 2020). Some natural and synthesized flavonoids have recently been selected for competitively binding to anxiolytic benzodiazepine receptors with increased risk of anxiolytic action (Aquino et al., 1987; Marder et al., 1996; Wolfman et al., 1996).

The forced swimming test is a rodent depression indication (Bogdanov et al., 2013). The depressed state is represented when mice become immobile after a period of vigorous activity. Depression is essentially defined in clinical terms as a pathological complex of psychological, neuroendocrine and somatic symptoms (Holmes et al., 2013). The test is conducted on the idea that the animal attempts, by vigorous swimming, to escape stressful stimuli. If the animal does not swim and floats to the surface, it displays a desperate situation. Normally, it is performed for 5 minutes in mice. The time when immobility is reached is recorded (Crawley, 2007). Increased activity, such as climbing or swimming and reduced immobility have been revised as behavioral characteristics compatible with the effect of an antidepressant (Cryan et al., 2002; Charles et al., 2018; Boublata et al., 2020). Antidepressants that inhibit serotonin and/or NA reuptake decrease immobility and increase swaying behavior in mice in the TST, a behavior that was not significantly altered in mice treated with MAE. Opiates are reported to reduce immobility and improve recirculation performance (Berrocoso and Mico et al., 2009; Berrocoso et al., 2013). In the forced swimming test the *C. arabica* plant increased swimming time in animals treated with ethanolic extract of *C. arabica* and decreased immobility time. The reduction in immobility time represents an antidepressant effect (Taiwo Adefunmilayo et al., 2012; Benneh et al., 2017; Benneh et al., 2018; Boublata et al., 2020). Antidepressants, including fluoxetine, selectively improve swimming behavior by means of serotonergic medications. In addition, FST enables for discrimination between antidepressant products operating with serotonergic or noradrenergic pathways (Dekte et al., 1995) and dual-acting drugs that increase both swimming and climbing (Reneric and Lucki, 1998). In this study, *C.arabica* plant resulted in an increase in immobility

time, an increase in swimming behavior, and an increase in climbing duration. This behavioral profile might may cause the mechanism of *C.arabica's* antidepressant activity and imply that a connection with noradrenergic and serotonergic systems.

The behavioral results of this study thus confirmed and extended the previous findings that the administration of the *C. arabica* plant had antidepressant-like effects. This confirms some previous studies (El Fazaa et al., 2000). Atchley (2011) showed that the activation of the hypothalamic-pituitary-adrenal axis (HPA pathway) was connected with stressful events. Furthermore, a broad spectrum of research shows that elevated HPA activities also affect the cognitive function of both rats and humans (Song et al., 2006; Maccari and Morley-Fletcher, 2007; Asia et al., 2007).

Serum creatinine and urea have usually been utilized for the diagnosis of renal damage (Edelstein, 2008).Our results show the *C.arabica* plant acts significantly on the level of blood glucose, urea, triglycerides and cholesterol in animals treated with this plant compared to other groups (Depoju and Odubena,2009; Samout el ., 2015; Ramdan et al., 2015 ; Boublata et al., 2020), The inclusion of phytochemicals (flavonoids, tannins, glycosides, sterols and saponin may cause the anti-diabetic effect of *C.arabica* (Arora et al., 2011). Antioxidant activities are assumed to have an anti-diabetic impact in plants which contain active inputs such as glycosides and flavonoids.*C. arabica* also includes a large number of organic sulfur compounds, and the sulfur derivatives' hypoglycemic effects are well known. Many sulfur plants have historically been utilized as anti-diabetic products (Lanjihiyana et al., 2012). Research has demonstrated that certain plant material is harmful to blood parameters and bone marrow when swallowed, whether raw or extracted (Omodamiro and Nwankwo, 2013). Neutropenia, thrombocytopenia, hemolytic

anemia, aplastic anemia and macrocytic anemia are mostly affected in order of frequency (Lubran, 1989). On the other hand, several plants also stimulate the blood and bone marrow parameters (Omodamiro and Nwankwo, 2013).

Hematological values are commonly utilized to examine systemic links and physiological adaptations, including evaluation of an organism's health overall (Tende et al., 2013; Oyedemi et al., 2011). The hematological testing of the hedging parameters is used not only to identify the detrimental effects of extracts on the blood of an animal, but also to explain the blood functions or products of a plant extract (Omodamiro et al., 2013). Toxic compounds, including the liver and kidneys, are carried by the blood to different organs, where they are potentially harmful. Blood can function as an animal pathology and physiology indication (Jorum et al., 2016). The bioactive chemicals have been recognized as possibly mediators of the health effects of medicinal plants.Administration of *C.arabica* resulted in the rats receiving an increase in the white blood cells (WBC). In Mistletoe Rats more white blood cells (WBCs) have been seen, while there has been no statistically significant increase.WBCs play a key function in protecting the body from infection and tissue damage. This validates earlier studies that mistletoe and various popular medicinal herbs contain substances which boost WBC formation (Al-Mamary, 2002; Imoru et al., 2005). This indicates that the extract can stimulate immunological activity on animals. Such effects may also have an increased permeability of the vasculature. Mistletoe extract injection appears to be activating the immuno system's effector cells. It is usually said that immune boosters enhance, harmonice and aid the immune system fight against invaders like germs and viruses Immune boosters (Bendich, 1993; Al-Mamary, 2002).

In the rats treated with the *C.arabica* plant, the Hb concentration was also greater than in the control group, indicating the suitable production in the blood and pigmentation. It means that in treated rats the capacity of oxygen to move the blood was higher than in the controls. This can be attributed to the fact that the extract of the *C.arabica* plant has the ability to improve erythropoiesis. Furthermore, the groups treated with the *C.arabica* had greater Hb levels. This is similar to the results of Egba et al., (2013) and Obeagu et al., (2013) when using *Telfairia occidentalis* leaf extract and those of Kadham (2008) using *Haloxylan salicornicum* aqueous extract. Treated rats recorded higher erythrocyte values than the control except for those treated with a dose of 200 mg / kg. The results of Dharmarathna et al., (2013) demonstrated that *Carica papaya* leaf extract increases red blood cell count in the mouse model to grow without generating any type of toxicity. Enhanced production of red blood cells can be an indicator of increased bone marrow activity and enough extract-induced erythropoieses (Cole, 1986). This will have to be confirmed in further studies. It appears that the herbal extract can have erythropoietic qualities which improve erythropoietics, as is also shown in the aqueous extract of the *Solanum torvum* fruits which increases both Red and Hb levels of phenyl hydrazine-induced anemic rats at dosages from 37.5 to 150 mg/kg (Koffuor et al., 2011).

We recorded non-significant effects of the extracts on the number of red blood cells in treated animals (Adebayo et al., 2006). Increased monocytes were shown in situations of infection; hence, decrease of monocytes may signal that there is little or no extract infection (Ashafa et al., 2011).

In animals treated with *C. arabica* plants we have seen an increase in lymphocytes and an average platelet volume. Dynamic cells and immunological responses to external chemicals include lymphocytes (Pearce et al., 2013). It also

produces antibodies that kill bacteria and cancer cells in intracellularly (Ganong, 2001). The rise in lymphocytes indicates that the plant has putative immunostimulating effects (Osei-Bimpong et al., 2012).

Organ weight changes are sensitive to toxic, enzyme effects, physiological disruptions, and organ damage in toxicity studies (Michael et al., 2007). Hypertrophy is shown by increasing the weight of organ whereas decreasing organ weight suggests necrosis (Teo et al., 2002). While organ weights give useful signals that show effects of the test item, organ weight data have to be analyzed in an integrated way with gross pathology, clinical pathology and histology results (Sellers et al., 2007).

The reduction in hepatitis seen in rats treated with *C. colocynthis* ethanol extract might indicate toxicity, the extract, which might be toxic to the liver in chronic usage (Ugwah-Oguejiofor et al., 2019).

The kidney is one of the major excretion organs. The testing is carried out almost exclusively in the evaluation of the renal function for creatinine tests that accidentally estimate the glomerular filtration rate. Creatinine in the kidney is routinely formed by the phosphocreatinine metabolism, which is released into the blood and ejected from the neuron as a metabolic waste. Ethanolic extract from *C.arabica* considerably lowered the levels of creatinine and urea relative to the control in the receiving groups. This is therefore consistent with the study of Muhammad (2015), who indicated that reducing the amount of creatinine and urea is hopeful or prospective for *M. pruriens*.

High plasma creatinine and urea levels might therefore be reduced. Consequently, the decrease of urea and creatinine in *M. pruriens* is a possible source of bioactive compounds to enhance renal function. The relative organ weight is a frequent toxicology index (Mouokeu et al., 2011). A toxicity assessment in animal models is regarded a more specific parameter than absolute weight (Jayesh et

al., 2017). A general sign of toxicity after hazardous exposure is a decreased internal organ weight (Boligon et al., 2016). Heart, liver, spleen, kidney and lung are major organ-related to toxins caused by metabolic processes (konate et al., 2012). After treatment with ethanol extract of *C.arabica* a substantial decrease of relative organ weight was detected, which indicate potential toxic effects on wistar rats (Amarasiri et al., 2020).

CONCLUSION

With the aim of proposing less toxic and more environmentally friendly substitutes in this study, the effect of the two ethanolic plant extracts on a non-target organism was proven. Both biopesticides studied caused behavioral disorders in Wistar rats due to the disruption of ACTH hormone levels. It seems that the extract of the Saharan plant *C. arabica* presents less risk compared to the lipid synthesis inhibitor (spirotetramat) and for this we recommend the use of bioactive molecules. This study indicates that the aqueous extract of *C. arabica* has an antioxidant effect and can be used as an antidiabetic treatment. The results of this work show that the plant acts on the levels of cholesterol, urea and creatinine observed in individuals treated with this plant. The extract of the *C. arabica* plant causes behavioral disorders in Wistar rats, reflected by disturbances in the levels of the hormone ACTH. It seems that the extract of the Saharan plant *C. arabica* presents less risk and for this reason we recommend the use of bioactive molecules from plants in the biological control of pests.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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