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Research Article
Comparative Toxicity Study of Novel Light-Activated Insecticide and Deltamethrin in Albino Rats

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Abstract

Background and Objective: Tri-sodium Copper of chlorophyllins (Agri-Safe) is a novel biocide using recently to control the mosquitoes as a larvicide. Because, the lack of adequate data on the toxicity of this compound, more toxicological studies on this new compound are necessary. Therefore the study aimed to evaluate the adverse effects of this new insecticide and in comparison with the traditional insecticide Deltamethrin (DM). **Materials and Methods:** Twenty-five adult male rats were randomly divided into five groups. The first group was kept in control. The second and third groups were administered at doses of 0.59 and 0.24 mg kg^{-1} b.wt., of DM. The fourth and 5th groups were administrated at doses of 250 and 100 mg kg^{-1} b.wt. of Agri-Safe respectively. The administrations were orally by gavage for 90 consecutive days. The rats were humanly sacrificed and whole blood was collected for hematological parameters and bone marrow was collected for mutagenicity assays. **Results:** The estimated LD_{50} of DM and Agri-Safe were 11.76 and more than 5000 mg kg^{-1} b.wt., respectively. Both insecticides induced slight hepatotoxicity but not nephrotoxicity. The high and low doses of DM induced prominent oxidative stress while Agri-Safe did not induce oxidative stress. The results of genotoxicity revealed that DM caused greater mutagenic effect at high and low doses, while Agri-Safe induced slight significant genotoxicity at high-dose only. **Conclusion:** It can be concluded that Deltamethrin (DM) can induce oxidative stress and prominent genotoxicity while tri-sodium copper of chlorophyllins has a low side effect and its effect is due to copper elements.

Key words: Copper complex of chlorophyllin, deltamethrin, oxidative stress, liver functions, kidney functions, mutagenicity

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

For centuries, pesticides have been used to control unwanted pests. The mosquitoes as one of the dangerous pests in the world, it's the most important carriers of disease worldwide, causing millions of human deaths each year[1]. A mosquito's life cycle includes four different phases: the egg, larva, pupa and adult. Mosquito control at each development stage needs different pesticides with different application methods[2]. Larviciding is the best application of chemicals to kill or inhibit the growth of the mosquito life cycle from developing into the adult[3]. Deltamethrin (DM) as one of the regular pyrethroid insecticides, is being used for wide-area control of adult mosquitoes of various species. However, there are probably mosquito populations resistant or less susceptible to this insecticide [4]. Besides, previous literature demonstrated deltamethrin has a mutagenicity effect, which can be dangerous to humans and non-target organisms. In *in vitro* studies, deltamethrin causes significant damage to chromosomes and this may be lead to cancer[5]. Also, the previous study reported that the free radicals induction by deltamethrin plays the main role in causing oxidative stress damage[6]. Therefore, a new generation of insecticides having a novel mode of action with high bioefficacy on insects and Safe to the environment is an essential request. One of these new modern insecticides is Tri-sodium copper of chlorophyllin as a new synthesis biocide. This compound which is protected by patent law is used as a unique model of controlling mosquitos. The new compound is called Agri-Safe® and consists mainly of copper complexes of chlorophyllins[7]. Chlorophyllin is a water-soluble salt produced by alkaline chlorophyll hydrolysis with copper substitution of magnesium. Besides, sodium or potassium substitution of the methyl and phytyl ester group[8]. The new mode of action of this compound depends on the insecticide that can be taken by mosquito larva in the feeding process. The accumulated compound in the larva tissue upon exposure to sunlight produces Reactive Oxygen Species (ROS) which is generated by energy transfer from excited triplet state to the ground state of oxygen within larva tissue. The cytotoxicity of Agri-Safe as mosquito's larvicide is due to photodynamic process and ROS stress reaction with biomolecules in the cell membrane of the larva and cell components[7]. Previous literature reported that no risks to the environment are expected from the use of copper complexes of chlorophyllins in animal nutrition[9]. However, the absence of adequate data on the toxicity of this compound imposes to do more toxicological studies about this new chemical and its metabolites. Besides, the Deltamethrin (DM) as a traditional insecticide used for a long time for controlling mosquitoes [10], is suitable to be used as a compared insecticide with this new model of insecticide.

Therefore, the present study was aimed to evaluate the adverse effects of subchronic toxicity of the new compound Agri-Safe and DM on adult male albino rats. Besides, to evaluate which one of them is more risk to human than the other. This research included several toxicological parameters ranging from acute toxicity, liver and kidney functions, mutagenicity assays and oxidative stress parameters.

MATERIALS AND METHODS

Study area: The study was carried out at the Department of Mammalian and Aquatic Toxicology, Central Agricultural Pesticides Lab, Giza, Egypt from February-April, 2020.

Tested Insecticides: The first insecticide (Agri-Safe®) is a liquid substance with an active ingredient of 99% of Tri-sodium copper complexes of chlorophyllins which are locally manufactured in Innovative Research and Development Incorporation (INRAD), Egypt. The second insecticide was Emulsifiable Concentrate (EC) with an active ingredient of 2.5% of Deltamethrin (DM). The last insecticide is the commercial formulation, sale and registered in Egypt and purchased from a local distributor.

Animals: A fifty healthy male Wistar strain albino rats weighing 140g±10% have been used in the study. The animals were obtained from the animal facility house of Mammalian and Aquatic Toxicology department, Central Agricultural Pesticides Lab, Giza, Egypt. The animals had five rats per cage, free access to fresh-water and a well-balanced, fresh diet. They were kept under observation two weeks before the experimental research began.

Experimental design

Median lethal dose (LD_{50}) study: The oral LD_{50} (median lethal dose) was calculated to provide initial information on the toxic nature of the formulations being tested. A total of 25 male rats were randomly divided into five groups, each of has five rats. The first and second groups were used as a pilot test of both tested insecticides. It is useful to determine the range of dose levels in the main study or an adequate limit test. The Agri-Safe insecticide did not need further main toxicity study Just a limit test has been performed. The other three groups were administered DM insecticide at three dose levels 5.6, 9.9 and 17.5 mg kg^{-1} b.wt., respectively. The rats were monitored

at least once within the first 30 min after dosing, then regularly over the first 24 hrs and for a total of observation period 14 days. The signs of toxicity and mortality were recording during the observation period. The calculation method of the LD_{50} was carried out according to the previous method Weil[11]. When the mortality data (R-values) were recorded, the f-values can be obtained from the tables. The LD_{50} can be calculated from the following Eq.:

$$\log m = \log D + d\,(f+1)$$

Where:

log m = Logarithm of the LD_{50}
log D = Logarithm of the lowest dose
d = Logarithm of the constant ratio (= 1.46) between dosage levels. The equation and f-values are included in this method

Subchronic 90-day oral toxicity study: Twenty-five adult male rats were randomly divided into five groups. The first group was held as control and provided only (1 mL (d/w)/100 g b.wt). The second and third groups were administered at doses of 0.59 and 0.24 mg kg^{-1} b.wt. of DM. The fourth and fifth groups were administrated at doses of 250 and 100 mg kg^{-1} b.wt. of Agri-Safe insecticide respectively. The administrations of tested insecticides were orally by gavage for 90 consecutive days. The high and low doses were equivalent to 1/10 and 1/30 of the estimated LD_{50} of each insecticide. The signs of toxicity and rat body weights were regularly recorded [12].

Blood samples and bone marrows collection: Rats were sacrificed euthanasia at the end of treatments. Blood samples were collected in sodium heparin tubes for plasma samples and then the samples were centrifuged at 2000 rpm for 10 min and stored at -20°C to be used for biochemical parameters. Both femurs were excised out and, the bone-marrow cells were collected from both femurs for mutagenicity assays according to the technique described later.

Biochemical parameters: In plasma samples, both liver and kidney functions and oxidative stress parameters were measured according to the information given in the kit's instructions, except some parameters were determined in whole blood and serum. All assays were performed by using a Jasco UV-VIS spectrophotometer V-630 PC (Japan).

Mutagenicity assay: Cytogenetic assays are carried out routinely to determine the mutagenic ability of tested chemicals. The micronucleus test (MNs) in bone-marrow cells serves as an important endpoint to detect the genetic damaged by chemicals in the cells of the organisms. The technique was performed according to the method described earlier by Schmid[13] with some modifications recommended by Krishna and Hayashi[14]. Besides, the identification of chromosomal damage provides a method for checking the genotoxic effects of chemical substances. The technique was conducted using a procedure defined earlier by Preston *et al.*[15].

Statistical analysis: One-way ANOVA and followed by the Bonferroni test were used to determine differences between groups for all parameters. The results are presented as mean±Standard error of the mean (SE). Values were considered statistically significant if $p<0.05$. The SigmaPlot statistics software, Ver.11 was used for the statistical analysis.

RESULTS

LD_{50} of DM and Agri-Safe insecticides: The estimated oral LD_{50} of DM was 11.76 mg kg^{-1} b.wt. for adult male rats. The symptoms of toxicity that were observed on the animals began to appear after 1 h of the administration. The main observed symptoms were slight tremors and bleeding from the nose. Finally, paralysis was happened and followed by death after 24 hrs from the administration. The recovery happened in some treated animals at low and middle doses after the observation period (14 days). On the other hand, the estimated oral LD_{50} of Agri-Safe insecticide was more than 5000 mg kg^{-1} b.wt., for adult male rats. No mortalities and no signs of toxicity on the treated animals were found during the observation period.

Effect on the body weights: After subchronic exposure, it was observed that both insecticides did not cause death or induce signs of toxicity on treated rats. However, there was an observed decrease in body weight gain in the DM treatments in the high-dose group but a weak increase in the low-dose group when compared to the control group. Nevertheless, Agri-Safe insecticide did not occur observed changes in the body weight gain in both high and low dose groups when compared to the control group (Table 1 and Fig. 1).

Effects on the liver and kidney functions: The high-dose of Agri-Safe insecticide treatment-induced some changes in liver functions which led to a significant increase in Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) levels in the high-dose group ($p<0.001$). The low-dose group

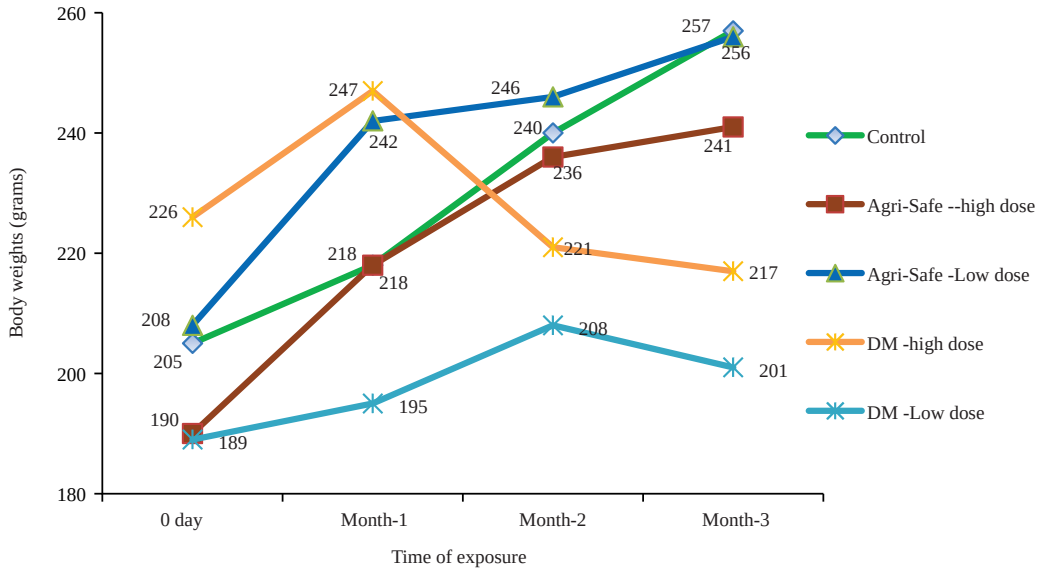

Fig. 1: Correlation between the exposure time and the mean of body weights of control and treatment groups

Table 1: Effect of DM and Agri-Safe treatments on body weight gain of treated rats as compared to control after 90 days of treatment

Treatments	Initial weight	Final weight	Net body weight gain*
Control group	205	257	25.37
DM			
Low dose	189	201	6.35
High-dose	226	217	(↓)-3.98
Agri-safe			
Low dose	208	256	23.08
High-dose	190	241	26.84

*Net body weight gain (gram) = ([final body weight-initial body weight]*100/initial body weight)

Table 2: Biochemical parameters in the plasma of rats treated with the DM and Agri-Safe

		Deltamethrin(DM)		Agri-Safe	
Parameters	Control group	Low	High	Low	High
AST (IU mL^{-1})	11.00±1.58	12.40±2.84	22.60±3.84(↑)*	21.00±0.84	29.60±4.12(↑)***
ALT (IU mL^{-1})	18.20±3.34	18.00±4.42	10.34±4.63	43.60±3.31(↑)*	34.40±3.34(↑)***
Alb (U L^{-1})	5.08±0.28	4.76±0.18	4.24±0.285(↓)*	5.30±0.20	4.29±0.01
Potassium (mmol L^{-1})	2.45±0.30	3.15±0.46	2.99±0.71	3.22±0.58	2.82±0.66
Sodium (mmol L^{-1})	240.32±40.44	378.71±85.56	320.43±91.32	415.78±65.87	331.05±97.62
Urea (mg dL^{-1})	5.82±0.59	5.93±0.64	6.17±0.81	6.17±0.69	5.01±0.65
Creatinine (mg dL^{-1})	0.423±0.02	0.53±0.09	0.38±0.035	0.46±0.019	0.31±0.06

Values are from five animals in each group and expressed as Mean±SE, ***Significant at p<0.001, **Significant at p<0.01, *Significant at p<0.05, (↑), Significant increase, (↓), Significant decrease, AST: Aspartate Aminotransferase, ALT: Alanine aminotransferase, Alb: Albumin levels

induced only a significant increase in ALT levels (p<0.05). The other biochemical parameters of liver functions albumin levels (Alb), potassium and sodium levels were not significantly changed when compared to the control group. On the other hand, the Deltamethrin (DM) treatments did not induce statistically significant liver biochemical parameters except at high-dose level induced a significant increase in AST levels (p<0.05) and a significant decrease in albumin levels (p<0.05). While the kidney function parameters (urea and creatinine levels) were not significantly changed in both doses of two tested insecticides when compared to the control group (Table 2).

Effects on the oxidative stress parameters: The results are summarized in Table 3 which indicated that the DM induced highly oxidative stress through a significant increase in the level of Total Antioxidant Capacity (TAC) at high and low doses (p<0.001). The levels of Catalase (CAT) at high and low doses were significantly decreasing (p<0.001). Also, the lipid peroxidation (MDA) and the level of Hydrogen Peroxide (HP)

Table 3: Assessment of oxidative stress parameters in the plasma of rats treated with the DM and Agri-Safe

		DM = (1/10 LD_{50}) low dose		Agri-Safe	
Parameters	Control group	Low	High	Low	High
TAC (mM L^{-1})	3.80±0.27	8.64±0.50(↑)***	8.03±0.41(↑)***	3.08±0.06	3.19±0.16
Cat (U L^{-1})	80.96±3.55	53.14±0.84(↓)***	50.26±2.89(↓)***	75.50±0.61	15.33±1.02
*GSH (U L^{-1})	16.07±1.83	18.07±0.80	18.03±0.87	17.79±0.74	5.82±0.59
GST (U L^{-1})	119.45±5.08	152.30±7.62	142.46±6.47	214.56±15.91(↑)***	169.73±12.62(↑)**
MDA (nmol mL^{-1})	11.02±0.27	23.75±0.76(↑)***	19.53±0.65(↑)***	11.11±0.64	10.17±0.30
HP (mM dL^{-1})	0.29±0.05	4.42±0.19(↑)***	4.34±0.19(↑)***	1.41±0.05(↑)**	1.51±0.10(↑)**

Values are from five animals in each group and expressed as Mean±SE, ***Significant at p<0.001, **Significant at p<0.01, *Significant at p<0.05, (↑), Significant increase, (↓), Significant decrease, TAC: Total antioxidant capacity, CAT: Catalase, *GSH: Glutathione reduced (in the whole blood) and GST: Glutathione-s-transferase, MDA: Malondialdehyde, HP: Hydrogen peroxide

Table 4: Numbers of micronucleus frequency in rats bone marrow cells after subchronic exposure of the DM and Agri-Safe

	Number of micronuclei in the cell				
Treatments	1	2	≥3	Total No. of micro-nucleated cells	Mean±SE
Control group	13	6	1	20	4.00±0.84
DM					
Low dose	41	28	10	79	15.80±3.57*
High-dose	69	42	17	128	25.60±3.23***
Agri-safe					
Low dose	34	12	9	55	11.00±1.82
High-dose	53	24	9	86	17.20±1.11**

Values are from 5 rats in each group and the last column represent Mean±SE of micronuclei per 1000 PCEs, ***Significant at p<0.001, **Significant at p<0.01, *Significant at p<0.05

Table 5: Chromosomal aberrations induced in rats bone marrow after subchronic exposure of the DM and Agri-Safe

	Types of structural aberrations				Numerical aberration	Total aberrant cells/250 scored	
Treatments	tg	R	C-A	C-T	(polyploidy)	metaphases	Mean±SE
Negative control	4	3	2	3	4	16	3.20±0.80
DM							
Low dose	5	9	8	2	8	32	6.40±0.812
High-dose	9	21	18	11	16	75	15.00±1.64***
Agri-safe							
Low dose	7	0	12	1	9	29	5.80±0.66
High-dose	8	7	11	4	9	39	7.80±0.58

Values are from 5 rats in each group and the last column represent Mean±SE of aberrant cells per 250 spread metaphases/treatment, ***Significant at p<0.001, **Significant at p<0.01, *Significant at p<0.05, tg: Chromatid gap, R: Ring chromosome, C-A: Centromeric attenuation, C-T: Chromosomes translocation

at high and low doses were significantly increased (p<0.001). While the Agri-safe did not induce any significant changes in the levels of TAC, CAT and lipid peroxidation (MDA). However, induced a significant increase in the activity of Glutathione-S-Transferase (GST) (p<0.01) and (p<0.05) at high and low doses respectively. Besides there is a significant increase (p<0.01) in the Hydrogen Peroxide levels (HP) at high and low doses. Nevertheless, the glutathione-reduced level (GSH) was not significantly changed in both insecticide groups at two dose levels when compared to the control group.

Mutagenicity effects: The micronucleus assay results are presented in Table 4 and evaluated by determination of micronucleated polychromatic erythrocytes (MNPCEs) in total immature erythrocytes. DM induced a significant increase in micronuclei frequency (MNs) at high and low doses (p<0.001) and (p<0.05), respectively. However, Agri-Safe induced a significant increase in (MNs) frequency at high-dose only (p<0.01) when compared to the control group. More addition, the structure of Chromosomal Aberrations (CAs) in the present study are presented in Table 5 and were scored as chromatid gap (tg), end to end association or ring chromosome (R), centromeric attenuation (C-A) and Chromosomes Translocation (C-T). The chromosomal aberrations were significant increase only at the high-dose group of DM (p<0.001) but Agri-Safe in both dose levels did not cause significant changes in (CAs) when compared to the control group. Furthermore, the observed numerical chromosomal aberration was polyploidy (>2n). The data also reflected a dose-dependent response. The data in Fig. 2a demonstrates

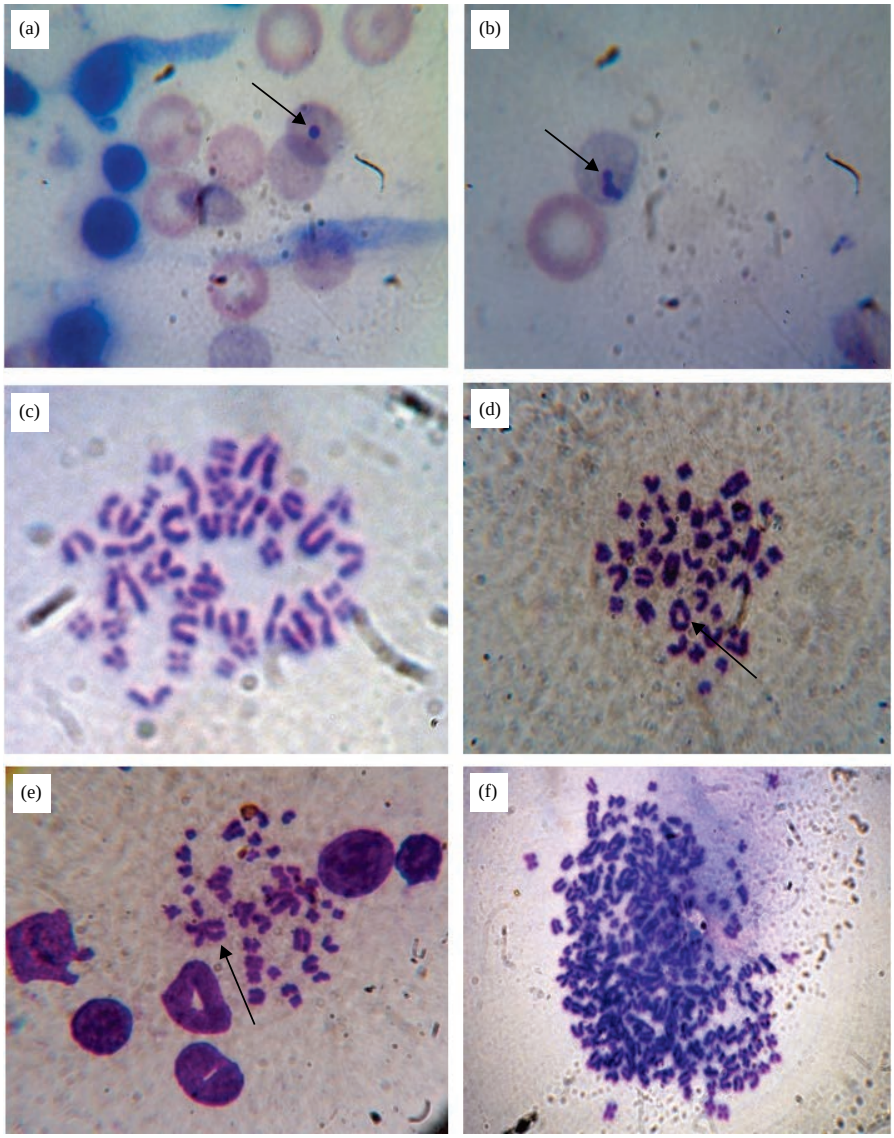

Fig. 2(a-f): Rats bone marrow photographs

(a) Polychromatic erythrocytes (PCEs) with one micronucleus, (b) With three micronuclei in PCEs, (c) Metaphase with centromeric attenuation, (d) Ring chromosome, (e) Chromosomes translocation and (f) Polyploidy(>2n)

MNPCEs with one micronucleus, Fig. 2b with three micronuclei in PCEs, Fig. 2c demonstrates metaphase with centromeric attenuation, Fig. 2d ring chromosome, Fig. 2e chromosomes translocation and Fig. 2f demonstrates polyploidy (>2n).

DISCUSSION

After the 90-days treatment with deltamethrin (DM) and Tri-sodium copper of chlorophyllin (Agri-Safe) insecticides, no mortality and no noticeable toxic signs were observed in treated rats. No obvious changes in body weight growth were observed in Agri-Safe treatment, while treatment with DM induced decreasing in the body weight gain. This result is in agreement with El-Gerbed[16] and Chargui *et al.*[17], who reported a decrease in body weight gain in rats exposed to DM. The decline in body weight gain in rats exposed to DM groups may be due to the increase in lipid and protein degradation as a result of the insecticide's toxic effects. Also, it could be due to the combination of many factors including oxidative stress and cholinergic effects[18]. The study further showed the DM induced a significant increase in AST levels only after the high-doses. These findings are in agreement with previous literature that reported deltamethrin treated rats showed significant increases in serum biochemical

parameters, including Aspartate Transaminase (AST), Alanine Transaminase (ALT), Alkaline Phosphatase (ALP) and these caused by inhibition of antioxidant enzyme activities[19]. Besides, our results showed no effect of DM treatment on kidney function and these findings coincide with Gündüz *et al.*[20] that found treatment with deltamethrin induced acute hepatotoxicity in albino rats but not nephrotoxicity. Additionally, oral treatment with deltamethrin for four weeks at 7.2 mg kg^{-1} b.wt., in female rats induced an increase in liver enzyme activities of AST, ALT, ALP levels and a decrease of catalase (CAT), Superoxide Dismutase (SOD) and Glutathione Peroxidase (GPx) activities [21]. But when discussing the Tri-sodium copper of chlorophyllin (Agri-Safe), the study showed an increase in liver enzymes (ALT and AST) after exposure to Agri-Safe and this may be due to the copper element which is one of the main components of this insecticide. While copper is completely essential for survival and plays a crucial role as a catalytic cofactor in mammals at the active protein site, such as cytochrome c oxidase, etc., Copper's excessive quantities can oxidize important biomolecules, such as lipids, proteins, DNA and cause adverse effects[22]. The results of this study are in line with Lee *et al.*[23] who reported the Copper nanoparticles (Cu NPs) caused liver and kidney injures with biochemical alterations, including increased AST, ALT, blood urea and creatinine. Also, the same results of Mladenovic *et al.*[24] reported the elevation of AST and ALT enzyme activities in the serum of copper-treated rats. Recently Abdel-Baky[25] found the rats treated orally with a daily dose of copper sulphate 100 and 200 mg kg^{-1} b.wt., revealed a significant increase in the activities of ALP, AST and ALT enzymes comparing with the control group. On the other hand, when discussing the oxidative stress effect of these insecticides, The key that causes the oxidative stress includes excessive development of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) as a consequence of the disturbed balance between ROS, RNS generation and antioxidant protection capacity Dasuri *et al.*[26] and Fujii *et al.*[27]. The excess ROS or RNS can damage cellular lipids, proteins and DNA resulting in inhibiting their normal functions[28]. In this study, the deltamethrin induced significant oxidative stress induction by decreases the catalase (CAT) activities and increases in lipid peroxidation by a significant increase of the (MDA) levels. Additionally, increases in total Antioxidant Capacity (TAC) and hydrogen peroxide. Although the hydrogen peroxide is a powerful oxidant at the center of many redox (reduction/oxidation) pathways, it also a key player in the healing process as neutrophil gathers in many bioreactions[29]. Our results are in coincide with the *in vitro* studies of Erdoğan *et al.*[30], who suggests deltamethrin may directly cause oxidative stress damage via ROS development. More addition, deltamethrin treatments with a dose of 1 and 5 μM induced cell death and ROS production in rat primary hepatocytes culture[31]. Besides, Mazmancı *et al.*[32] mentioned that one of the main mechanisms of deltamethrin toxicity is the induction of oxidative stress in treated rats via ROS generation. Previous results suggested the relationship between oxidative stress induction and ROS generation induced by deltamethrin is strong. Although preliminary research has established that ROS and RNS development are responsible for deltamethrin triggered oxidative stress and associated toxicity, the exact explanation of how deltamethrin increases ROS and RNS development remains uncertain and needs more further investigation[33]. On the contrary, the Agri-Safe did not induce oxidative stress at high and low doses except for significant increases in hydrogen peroxide and glutathione-S-transferases. These investigations are in agreement with the Lushchak[34], who reported that the excessive concentrations of copper in aquatic animals caused an increase in the glutathione-S-transferase activities and a decrease in the catalase activities. The increase activity of Glutathione-S-Transferase (GST) which is a multifunctional enzyme plays a key role in cellular detoxification. Therefore, the main effect of Agri-Safe insecticide is due to the main element copper and its metabolites. More addition, free Copper ions can be involved in ROS generation, by react with hydrogen peroxide H_2O_2 to produce hydroxyl radicals via the Haber-Weiss reaction and increases the ROS generation[35]. Likewise, the mutagenicity results of the present study demonstrate the mutagenic effect of DM which was significant increases in micronucleus frequency at high and low doses and significant increases in CAs at high-dose. These findings are agreements with Ncir[21] that reported deltamethrin treatment to female rats caused increases of oxidative stress and micronucleus formation. Further, deltamethrin treatments 7.2 mg kg^{-1} b.wt. (i.p.) for 2 weeks induced DNA fragmentation in liver tissue as compared to control group[36]. From the previous findings and the results of our study, it may suggest the deltamethrin induces its mutagenic effect through oxidative stress mechanism, because DNA damage induced by deltamethrin appears to be dose-dependent. This likelihood is agreement by Ansari *et al.*[37] that assumed oxidative stress induced from exogenous substances may potentially attack DNA and stimulate genotoxicity, including micronucleus induction, chromosomal and nuclear alterations and DNA breaks. Although many literatures support this hypothesis, the mechanism remains unclear. On the other hand, Agri-Safe did not induce significant increase in CAs at high and low doses but induces

slight significant increases in micronucleus frequency at high-dose only. Copper readily attaches to DNA in order to form DNA adduct. The endogenous DNA-associated copper may promote local development of hydroxyl radicals and the last one promotes more oxidative DNA damage[38]. Furthermore, the mutagenicity of copper compounds has been reported in many previous literatures by Prá *et al*.[39] that reported Copper induced high mutagenic effect as evaluated by comet assay and micronucleus test. Also, Mostafa *et al*.[40] investigated the copper chloride exposure can induce oxidative stress and genotoxicity in adult male albino rats after short term exposure. As above-mentioned these results impose the main side effect of Agri-Safe is due to the excessive copper element and its metabolites. In this study, the maximum tolerated daily dose of Agri-Safe insecticide was used, to record the maximum side effects can be obtained from treatment. Furthermore, when applied this bio-insecticide in the environment the residues of this insecticide that can be reached to the human or non-target organisms is very low. Therefore, tri-sodium copper of chlorophyllins (Agri-Safe) may be relatively safe from the environmental perspective as larviciding in controlling of mosquito, while there are some risks regarding uses of deltamethrin as a traditional insecticide especially its excessive uses in last years.

CONCLUSION

It can be concluded that deltamethrin (DM) can induce oxidative stress and prominent genotoxicity. deltamethrin should be used moderately as soon as possible to save human and non-target organisms. While tri-sodium copper of chlorophyllins (Agri-Safe) has low side effects and its adverse effect is due to the excessive of copper elements. According to this study, Agri-Safe is safer than deltamethrin and can be used safely in the environment to control mosquitoes.

SIGNIFICANCE STATEMENT

This study discovers the new and novel mode of action of Tri-sodium copper of chlorophyll as a new light-activated insecticide. Its efficacy depends on sunlight activation to produces reactive oxygen species in larva tissue and lead to kill the larva. This study declared the safety of this new compound when compared to the traditional insecticide. This study will help the researcher to explore new safe and effective compounds that derivatives from chlorophyll.

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