ACTA SCIENTIFIC NUTRITIONAL HEALTH

Volume 2 Issue 11 November 2018

Research Article

Cypermethrin and Medicinal Plant Antagonist Effects on Glycaemia in Healthy Animal Model

Abdelkrim Berroukche[1]*, Mohamed Terras[1], Abdelkader Ammam[2], Hafsa Dellaoui[2], Wassila Lansari[2] and Imen Zerarki[2]

[1]Research Laboratory of Water Resources and Environment, Biology Department, Faculty of Science, Tahar-Moulay University of Saida, Algeria

[2]Laboratory of Bio toxicology, Pharmagnosy and Biological Valorization of Plants, Biology Department, Faculty of Science, Tahar-Moulay University of Saida, Algeria

***Corresponding Author:** Abdelkrim Berroukche, Research Laboratory of Water Resources and Environment, Biology Department, Faculty of Science, Tahar-Moulay University of Saida, Algeria.

Received: October 15, 2018; **Published**: October 26, 2018

Abstract

Uncontrolled and excessive uses of insecticides, in agriculture, will expose the human and animal health to a high risk of chemical toxicity. Cypermethrin (CYP) is widely handled in tomato growing fields in Algeria. In addition to brain and lung tissue damage, CYP induced metabolic disorders. Medicinal plants widely used, as folk remedies, by rural population. This study aimed to compare both medicinal plant and CYP effects on blood glucose level in rats. Experiments conducted in 30 days, on 70 rats, divided into seven groups: NC, CYP (20 mg/kg), CYP-AHA, MC, EC, CV and OC. CYP and aqueous plant extracts (as hot decoction at 50 g/L) were orally administered to animals. A significant difference in body weight gain was reported (respectively 54.67, 15,39.67,12.65,8.34,39.63 and 4.66 g). No significant different results found about blood glucose levels and their mean values were respectively 0.82 ± 0.01, 0.94 ± 0.03, 1.51 ± 0.17, 0.73 ± 0.08, 0.72 ± 0.05, 0.71±0.03 and 0.81 ± 0.02 g/L. Furthermore, serum levels of renal markers showed slight variation such as urea (respectively 0.66 ± 0.02, 0.61 ± 0.05, 0.83 ± 0.03, 0.47 ± 0.13, 0.52 ± 0.05, 0.72 ± 0.01 and 0.44 ± 0.2 g/L) and creatinine (respectively 7.4 ± 0.2, 8.17 ± 0.14, 9.6 ± 1.25, 6.56 ± 1.38, 7.13 ± 0.07, 7.63 ± 0.64 and 8.23 ± 0.08 mg/L). Medicinal plants, used in this study, showed more or less significant hypoglycemic effects in contrast to CYP slightly hyperglycemic. Other studies are expected to consolidate this thesis.

Keywords: Insecticides; Cypermethrin; Metabolic Disorders; Medicinal Plants; Blood Glucose

Abbreviations

CYP: Cypermethrin; NC: Normal Controls; AHA: Artemesia Herba Alba; EG: Eucalyptus Globulus; OS: Ocinum Sanctum; MC: Myrtus Communis; CV: Cinnamommum Verum; MP: Medicinal Plant; SEM: Standard Error of Mean

Introduction

Pyrethroid insecticides, widely used in agriculture due to their high effectiveness against insects, low toxicity to mammals and easy biodegradability [1]. Perythroids are potential endocrine disruptors inducing irritation, headache, nausea and paresthesia [2]. Pyrethroid acute toxicity was established in brain, heart, liver kidney and testis tissues [3]. Few studies were performed on association of chronic perythroid toxicity with hyperglycemia [4]. Among perythroids, cypermethrin (CYP) is widely used in Algeria. CYP is widely used in agricultural, public health and domestic applications [5]. CYP found as trace in soil and water with half-life ranges between 2 and 165 days. CYP could be toxic through dermal exposure, ingestion and inhalation [6]. Several studies suggested that CYP acute toxicity induced syndrome of chrea salivation [6]. In studies led on mice, CYP chronic toxicity revealed genotoxicity in spleen and bone marrow whereas in human it was noted benign lung adenomas [7]. CYP is hydrophobic and interacts with proteins and phospholipids of cell membrane. CYP toxicity generates reactive oxygen species (ROS) and oxidative stress [8]. CYP is metabolized in liver through oxidative stress pathway by P-450 enzymes generating thus ROS triggering damage lipids, DNA and cell death [9]. Currently, studies are investigating whether there is an

association of insecticide toxicity with hyperglycaemia or diabetes [10]. Incidence of diabetes increased in worldwide displaying approximately 490 million diabetics [11]. Emerging evidence showed pesticides play main role in the pathogenesis of diabetes. Organochlorine pesticides (OCPs) and polychlorobephenyls (PCBs) directly associated with incident diabetes [12]. However, evidence to date has been inconsistent and outcomes are controversial about association pesticides-diabetes risk [13]. Inverse correlation has been established between medicinal plants effects and toxic effects of environmental contaminants. Aromatic plants are main source of bioactive substances such as phenolic acids, polyphenols and flavonoids. These compounds have anti-glycation properties allowing prevention and management of diabetes [14]. Phenolic compounds are involved in glucose metabolism through various mechanisms as glucose absorption in the intestine, stimulation of insulin secretion from pancreatic β-cells, modulation of glucose release from the liver, activation on insulin receptors and glucose uptake in the insulin-sensitive tissues [15]. Cell mechanisms of polyphenol hypoglycemic effects remains unclear. Flavonoids have antioxidant, anticancer, anti-allergic, anti-inflammatory and gastro-protective properties [15]. In this project, we assessed cypermethrin and medicinal plant effects on glycaemia in healthy rats.

Materials and Methods

Chemicals

Cypermethrin (CYP 97% purity) was purchased from local market, imported from TASMID industry, Tunisia.

Plant material

A single plant was purchased from local market and four plants were harvested at different Algerian areas, namely:

Artemesia herba alba (AHA), *Eucalyptus globulus* (EG), *Ocinum sanctum* (OC) and *Myrtus communis* (MC) were collected during period 2017 from Saida province (located in Western Algeria; latitude 34°50'00" N; longitude 0°09'00" E, altitude 868 m) and Tlemcen province (located in Western Algeria; latitude 34°52'41" N; longitude 1) 18'53"W, altitude 811 m).

Cinnamommum verum (CV) was purchased at local market (Saida, western Algeria).

Plants were authenticated, reference numbers have been assigned to them and deposited in Laboratory of Water resources and Environment, Biology Department, Faculty of Science, University of Saida, Algeria.

Preparation of aqueous extracts (decoctions)

Powdered AHA, EG and MC leaves (50 g/each plant) and bark CV (50g) were dissolved in boiled water (1000 mL/each plant) and left for 30 minutes to facilitate polyphenol extraction. Decoctions were filtered and stored at - 20°C.

Preparation of animals

Seventy adult male rats, weighting 120-200g, were purchased from Pasteur Institute, Algiers, Algeria. Animals were placed under the controlled conditions: 25°C, 12 hours light/dark cycle and free access to diet and water ad libitum. Animal experiments were conducted in accordance with the guidelines for the care and use of laboratory animals, published by the US National Institutes of Health (NIH Publication 85-23 revised 1996) and approved by the local ethical committee (University of Saida, Algeria).

Experimental design

Animals were divided into 7 groups (10 rats/group):

- **NC:** normal controls rats fed with standard diet and distilled water.
- **CYP:** rats orally administered with cypermethrin at dose 20 mg/ kg (< 1/10 LD50) dissolved in corn oil.
- **AHA-CYP:** rats, exposed to CYP, orally treated with *Artemesia herba alba* leaves decoction (1 mL ~ 340 mg/ mL).
- **MC-CYP**: rats treated with *Myrtus communis* leaves decoction in the same experiment conditions (1 mL ~ 340 mg/mL).
- **EG-CYP:** rats treated with *Eucalyptus globulus* leaves decoction in the same experiment conditions.
- **CV-CYP:** rats treated with *Cinnamommum verum* bark decoction (1 mL ~ 340 mg/mL).
- **OS-CYP:** rats treated with Ocinum sanctum leaves decoction in the same experiment conditions.

Biochemical study

Body weight of animals (g) and blood glucose (mg/dL) were measured every 7 days. Serum urea (mg/dL) and creatinine (mg/L) levels were determined every 10 days. Animals fasted overnight, blood samples collected from tail tip to measure glycaemia and blood drawn from heart under anesthesia to measure urea and creatinine levels. Blood glucose levels were measured by means of Bionime GM550 glucometer (Bionime Corporation, Taiwan, China). Blood glucose test based on glucose oxidase method. Serum urea and creatinine levels were measured using an automate-analyzer "Mini-VIDAS" (Bio Merieux laboratory, Lyon, France).

Statistical analysis

Data were expressed as mean ± SEM with $P < 0.05$ considered statistically significant. Statistical measurements were performed by ANOVA followed by the Tukey's test for multiple comparisons. Statistical software SIGMAPLOT (Version 11.0) was used.

Results and Discussion

Table 1 shows results of CYP toxic effects on weight and biochemical parameters in healthy animals. As seen in table 1 and figure 1, results of body weight and body weight gain are highly statistically significant ($p < 0.001$). At the dose (340 mg/kg/day): Medicinal plant aqueous extracts (*Myrtus communis, Eucalyptus globulus, Cinnamommum verum* and *Ocinum sanctum*) showed in animals, exposed to Cypermethrin (at < 20 mg/kg/day), following effects; hypoglycemia and lowering serum levels of creatinine and urea (Table1, Figures 2 and 3).

Groups of animals	BW(g) ± SEM	BWG (%)	Glycaemia (mg/dL)	Urea (mg/dL)	Creatinine (mg/L)
NC	189.72 ± 5.92	1.82	82.1 ± 4.9	66 ± 0.5	74 ± 11.50
CYP	198.27[a] ± 5.16	0.5	94 ± 4.2	61 ± 0.0	81.7 ± 5.7
AHA-CYP	167.66 ± 6.95	1.32	151[a] ± 8.3	83.6 ± 4.0	96 ± 17.3
MC-CYP	197.22 ± 1.39	0.42	73.1[a] ± 7.3	47 ± 5.7	65.5 ± 5.7
EG-CYP	153.10[a] ± 4.48	0.27	72.1[a] ± 7.3	52.3 ± 2.3	71.3 ± 17.3
CV-CYP	161.04 ± 4.24	1.32	71[a] ± 6.5	72 ± 1.5	76 ± 4.3
OS-CYP	151.83[a] ± 0.85	0.15	81.4[a] ± 2.9	44 ± 10	82.3 ± 5.7

Table 1: Mean values of weight and biochemical parameters.

Results are in Mean ± Standard error of means (SEM). Means with the same superscript at shows that there is high extremely significant difference ($p < 0.001$).

CYP and AHA-CYP groups displayed slightly increase in blood glucose levels (Table 1). *Artemesia herba alba* aqueous extract, in presence of CYP, didn't show hypoglycemic effect at same dose (340 mg/kg), likewise for other biomarkers (urea and creatinine). Antagonist and toxic effects of CYP were dominated and banned by the protective and antioxidant effects of plants (MC, EG, CV and OS) at used dose (340 mg/kg). These outcomes allow to think whether a dose (340 mg/kg), in *Artemesia herba alba*, was insufficient to trigger a hypoglycemic effect in the presence of CYP or maybe synergistic and combined effects of CYP and AHA are involved in increase of blood glucose.

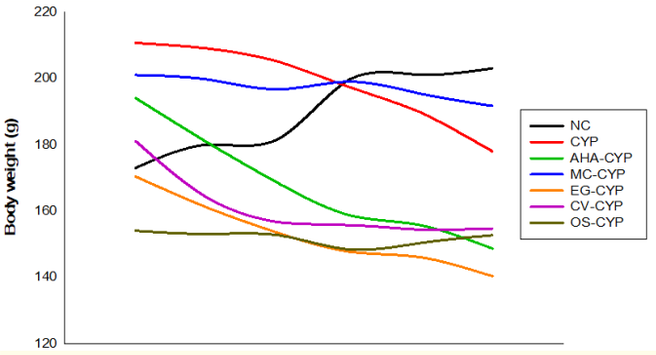

Figure 1: Variation of body weight in animals exposed to CYP and treated with medicinal plants.

To date, previously studies showed no strong association CYP-diabetes [16]. This study, used CYP at dose less 200 mg/kg, showed; CYP-induced slight hyperglycemia (94 mg/dL) compared to NC (82 mg/dL), CYP-mediated insignificant changes in urea and creatinine (respectively 61 mg/dL and 8.17 mg/L) compared to NC (66 mg/dL and 7.4 mg/L) (Table 1, figures 2 and 3). Ghorzi., et al. (2017) showed, in rats exposed to CYP (250 mg/kg); Hyperglycemia (142 - 194 mg/dL), Urea (40 - 77 mg/dL) and Creatinine (19 - 22.5 mg/L) [16-21].

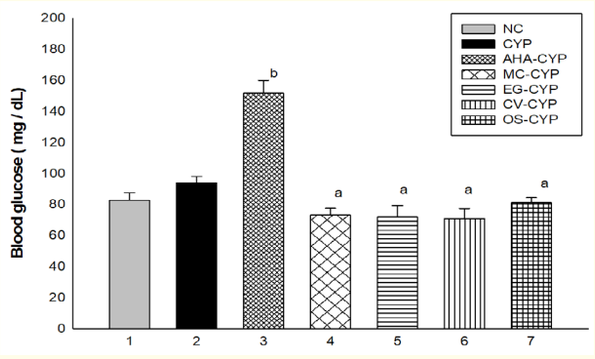

Figure 2: Variation of blood glucose in animals exposed to CYP and treated with medicinal plants.

b: highly significant difference between AHA-CYP and groups (MC-CYP, EG-CYP, CV-CYP and OS-CYP)

a: no significant difference between groups; MC-CYP, EG-CYP, CV-CYP and OS-CYP.

These outcomes are consistent with other studies conducted on the same medicinal plants. This work presented more or less similar results (Table 2).

Medicinal plants	Animals	Medicinal plants extracts	Medicinal Plant dose (mg/kg)	Duration (days)	Glycaemia (Controls) (mg/dL)	Glycaemia (diabetic rats) (mg/dL)	Glycaemia (diabetic rats treated)	Authors, year
AHA	Rats	Aqueous	390	10	114.80	265	263.10	Tastekin., *et al.* 2006 [17].
MC	Rats	Alcoholic	300	15	100	500-600	120-350	Malekpour., *et al.* 2012 [18]
EG	Rats	Alcoholic	130	15	149	267	192	Soussi., *et al.* 2009 [19].
CV	Rats	Aqueous	200	45	90.1	192.2	163.40	El-Desoky., *et al.* 2012 [20].
OS	Rats	Aqueous	1000	14	60.23	260.5	240	Mousavi., *et al.* 2016 [21].

Table 2: Comparison the outcomes of the present study with literature.

MP: medicinal plant; NC: normal controls; AHA: *Artemesia herba alba*; MC: *Myrtus communis*; EG: *Eucalyptus globulus*; CV: *Cinnamommum verum*; OS: *Ocinum sanctum*.

Conclusion

Results of this present study revealed, at low dose of Cypermethrin (20 mg/kg), that insignificant changes in biochemical parameters were occurred. Through this study, we could suggest that CYP didn't induce severe hyperglycaemia, not even diabetes. CYP, at low dose, is safe for farmers, for that CYP is most used pesticide in Algeria. Medicinal plants are not all hypoglycemic and there is insufficient evidence to determine their effectiveness. Their therapeutic potential may be limited. There is a natural and fair balance between CYP, which protects our agricultural fields against pests, and medicinal plants that are not all remedies. We conclude a natural and just equation.

Acknowledgements

Authors would like to thank the paramedical team of the biological laboratories of Saida hospital, Algeria.

Conflict of Interest

Authors declare that they have no competing interests.

Bibliography

1. Prusty AK., *et al*. "Synthetic pyrethroids (type II) and freshwater fish culture : perils and mitigations". *International Aquatic Research* 7 (2015): 163-191.

2. Ahmed M., *et al*. "Deleterious effects of cypermethrin on semen characteristics and testes of dwarf goats (*Capra hircus*)". *Experimental and Toxicologic Pat*hology 61 (2009): 339-346.

3. Sankar P., *et al*. "Protective effect of curcumin on cypermethrin-induced oxidative stress in Wistar rats". *Experimental and Toxicologic Pathology* 64 (2012): 487-493.

4. Gamet-Payrastre L and Lukowicz C. " Impact of pesticides mixtures". *Cahiers de nutrition et de diététique* 52 (2017): 234-238.

5. Wolansky MJ, *et al*. "Relative potencies for acute effects of pyrethroids on motor function in rats". *Toxicological Sciences* 89 (2006): 271-277.

6. Burr SA. "Cypermethrin". *Elsevier* 1 (2005): 714-716.

7. Kumar S., *et al*. "Demonstration of sperm head shape abnormality and clastogenic potential of cypermethrin". *Journal of Environmental Biology* 25 (2004):187-190.

8. Rizzati V., *et al*. "Effects of pesticide mixtures in human andanimal models: an update of the recent literature". *Chemico-Biological Interactions* 254 (2016): 231-246.

9. Svendsen C, *et al*. "Similarity, independence, or interac-tion for binary mixture effects of nerve toxicants for the nematode *Caenorhabditis elegans*". *Environmental Toxicology and Chemistry* 29.5 (2010):1182-1191.

10. Hernandez AR., *et al*. "An estimation of the carcinogenic risk associated with the intake of multiple relevant carcinogens found in meat and charcuterie products". *Science of the Total Environment* 514 (2015): 33-41.

11. Danaei G., *et al*. "National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants". *Lancet* 378 (2011): 31-40.

12. Robledo C., *et al*. "Is bisphenol-A exposure during pregnancy associated with blood glucose levels or diagnosis of gestational diabetes?" *Journal of Toxicology and Environmental Health* 76.14 (2013): 865-873.

13. Luzardo OP., *et al.* "Increasing serum levels of non-DDT-derivative organochlorine pesticides in the younger population of the Canary Islands (Spain)". *Science of the Total Environment* 367. 1 (2006): 129-138.

14. Elosta A., *et al*. "Natural products as anti-glycation agents: Possible therapeutic potential for diabetic complications". *Current Diabetes Review* 8 (2012): 92-108.

15. Xinyan B, *et al*. "Spices in the management of diabetes mellitus". *Food Chemistry* 217 (2017): 281-293.

16. Ghorzi H., *et al*. "Long term biochemical changes in offspring of rats fed diet containing alpha-cypermethrin Pesticide". *Biochemistry and Physiology* 142 (2017): 133-140.

17. Taştekin D., *et al*. "Hypoglycaemic effect of *Artemisia herba-alba* in experimental hyperglycaemic rats". *Bulletin of the Veterinary Institute in Pulawy* 50 (2006): 235-238.

18. Malekpour A., *et al.* "Effects of the Hydro-Ethanol Extract of *Myrtus communis* L. On Blood Glucose Level and Histopathological Changes in Alloxan-Induced Diabetic Rats". *Middle-East Journal of Scientific Research* 12.4 (2012): 517-522.

19. Soussi A., *et al.* "Oral administration of *Eucalyptus globulus* extract reduces the alloxan-induced oxidative stress in rats". *Chemico-Biological Interactions* 181 (2009): 71-76.

20. El-Desoky GE, *et al*. "Antidiabetic and hypolipidemic effects of Ceylon cinnamon (*Cinnamomum verum*) in alloxan-diabetic rats". *Journal of Medicinal Plants Research* 6.9 (2012): 1685-1691.

21. Mousavi L., *et al*. "Hypoglycemic and anti-hyperglycemic study of Ocimum sactum leaves extract in normal and streptozotocin-induced diabetic rats". *Asian Pacific Journal of Tropical Biomedicine* 6.12 (2016): 1029-1036.

Volume 2 Issue 11 November 2018