

Hematological and Biochemical Effects of the Aqueous Extract of the Phytotherapeutic Formulation Zigarda in Balb/c Mice

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ABSTRACT

Background: Zigarda is a phytotherapeutic formulation composed of three plants with multiple recognized medicinal properties.

Objective: To evaluate its effects on hematological and biochemical parameters in Balb/c mice.

Methods: Eighteen mice were divided into three groups: control (distilled water), Zigarda 200 mg/kg, and Zigarda 400 mg/kg, administered orally for 30 days. Body weight, hematological and biochemical parameters were monitored.

Results: Our results showed a slight increase in weight and a highly significant ($p < 0.001$) stimulation of leukocytes, suggesting an immunostimulatory effect. A significant decrease ($p < 0.05$) in red blood cells and platelets was observed, as well as a significant increase ($p < 0.05$) in liver enzymes, which may indicate a potential risk to the liver. Lipidemia showed a biphasic effect, with significant hypolipidemic potential ($p < 0.05$).

Conclusion: The phytotherapeutic formulation Zigarda has therapeutic benefits, particularly immunostimulatory and metabolic.

Keywords: Zigarda, Immunostimulation, Lipid-lowering effect, Balb/c mice.

INTRODUCTION

Zigarda is a phytotherapeutic formulation made from three plants commonly used by local populations and traditional practitioners. Each of these plants has remarkable medicinal properties, such as anti-inflammatory, neuroprotective, immunostimulant, antimicrobial, antiparasitic, antiviral, antifungal, and purgative effects. Traditional medicine and traditional therapists play an important role in providing care to populations. Traditional, complementary, and alternative medicines offer many advantages^{1,2}. More than 80% of the world's population, mainly in southern countries, depend on traditional herbal medicines for their healthcare needs³. The plants that make up Zigarda are functional foods that are frequently consumed around the world. In West and Central Africa, these plants play a major role thanks to their main nutritional components⁴. However, very few phytotherapeutic formulations are listed in the literature and have been studied^{5,6}. Hence the interest in promoting this phytotherapeutic formulation. The objective of our study was to evaluate the effects of the

aqueous extract of the phytotherapeutic formulation Zigarda on hematological and biochemical parameters in Balb/c mice.

MATERIALS AND METHODS

Plant material

The aqueous extract based on the Zigarda phytotherapeutic formulation was obtained by cold maceration with stirring of 50 g of powder from the phytotherapeutic formulation in 500 ml of solvent (distilled water) for 72 hours. The mixture of plants constituting the phytotherapeutic formulation was balanced. Evaporation was performed using a BUCHI Rotavapor R-100.

Animals and housing conditions

Eighteen female Balb/c mice from the animal facility of the Faculty of Health Sciences were used. They were kept in their natural habitat, with free access to food and drinking water ad libitum. This experimental study was conducted in accordance with Directive 2010/63/EU on the protection of laboratory animals ⁷.

Methods

The laboratory work consisted of investigating the effects of prolonged treatment with the phytotherapeutic formulation Zigarda on hematological and biochemical parameters in Balb/c mice.

Treatment

Treatment consisted of oral administration of the various products at their respective doses for thirty days. For our study, three groups of animals were formed and treated. The first group received distilled water at 0.1 ml/kg and served as the control group. The second group was treated with Zigarda at a dose of 200 mg/kg. The third group was treated with Zigarda at a dose of 400 mg/kg.

Sample collection

Blood was collected from the retro-orbital sinus at the end of the treatments. After determining the hematological parameters, the samples were centrifuged at 3,000 rpm

for 4 minutes and the biochemical parameters were measured.

Determination of changes in weight, hematological and biochemical parameters

The animals' weight was recorded during the treatment phase. Weight and blood parameter assessments can be used to determine the level of side effects or adverse reactions to various substances, including medicinal plant extracts. Blood counts and leukocyte formulas were performed using a Yumizen H550 hematology analyzer from Horiba Medical. This is a hematology counter capable of performing 43 complete blood count tests per hour with qualification of immature elements (percentages of neutrophils, basophils, eosinophils, and lymphocytes) based on the principles of white blood cell detection and differentiation. EDTA tubes containing whole blood from Balb/c mice were sent for hematological analysis. Serum biochemical parameters (high-density lipoprotein cholesterol, alanine aminotransferase, aspartate aminotransferase, blood glucose, and total cholesterol) were measured using commercial kits from Biomérieux on the CYAN® analyzer. Various methods were used to determine, among other things, the concentration of triglycerides (TG), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). These included the two-point kinetic method and the end-point enzymatic method ⁸.

Statistical analysis

The results were expressed as means plus standard deviation. Statistical analysis was performed using Statistical Package for Social Science (SPSS) version 20 after data entry in Excel 2019. One-way ANOVA followed by a post-hoc test (Tukey) was performed. Comparisons of non-progressive parameters were performed using Student's t-test. The significance threshold corresponds to a risk of error * $p < 0.05$.

RÉSULTATS

Body weight

Zigarda was administered orally for 30 days at doses of 200 and 400 mg/kg to Balb/c

mice. Figure (1) illustrates the change in body weight of Balb/c mice.

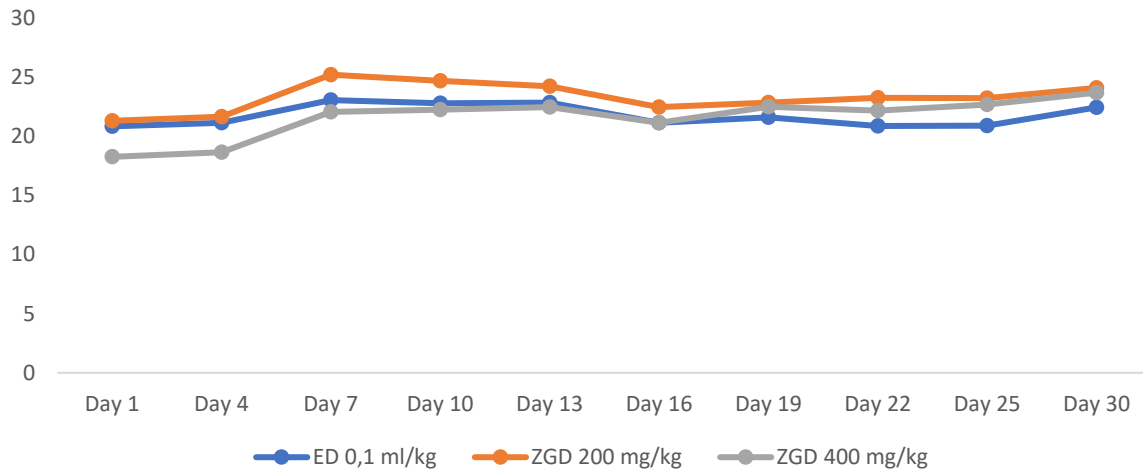


Figure 1. Effects of Zigarda on the body weight of Balb/c mice

Hematological parameters

Zigarda was administered orally for 30 days at doses of 200 and 400 mg/kg to Balb/c

mice. The effects observed on hematological parameters are presented in Table (I).

Table I. Effects of Zigarda on hematologic parameters

Parameters	Lots		
	ED 0,1 ml/kg	ZGD 200 mg/kg	ZGD 400 mg/kg
GR	10.78 ± 0.89	10.32 ± 0.34	9.10 ± 0.93 *
HB	14.35 ± 0.93	14.65 ± 0.53	12.7 ± 1.42
HT	43.05 ± 1.93	43.95 ± 0.78	38.1 ± 2.69 *
VGM	40 ± 1.64	42.75 ± 1.19 *	41.9 ± 1.58
TCMH	13.38 ± 0.94	14.2 ± 0.39	13.93 ± 0.76
CCMH	33.33 ± 0	33.33 ± 0	33.33 ± 0
IDR-CV %	11.7 ± 0.59	12.1 ± 0.93	11.7 ± 1.06
IDR-SD	24.8 ± 0.73	26.9 ± 1.57	25.6 ± 4.09
PLA	1065 ± 260.52	1188.25 ± 129.47	688.5 ± 123.31*
THT %	0.24 ± 0.04	0.28 ± 0.02	0.15 ± 0.02 *
VMP	6.35 ± 0.17	6.8 ± 0.39	6.7 ± 0
IDP	21.12 ± 29.25	7.45 ± 0.93	7.7 ± 0.59
P-LCC	46.5 ± 1.73	74.22 ± 5.85 ***	40.5 ± 6.59
P-LCR %	5 ± 1.32	8.15 ± 1.73 *	5.9 ± 0.25
GB	3.24 ± 0.01	4.55 ± 0.44 **	7.44 ± 0.82 ***
NEU	0.57 ± 0.06	1.54 ± 0.62 *	1.43 ± 0.11 ***
LYM	2.52 ± 0.08	2.65 ± 0.93	5.92 ± 0.41 ***
MON	0.02 ± 0.02	0.13 ± 0.08 **	0.05 ± 0.02
EOS	0.03 ± 0.02	0.02 ± 0.01	0.03 ± 0.02
BAS	0.04 ± 0.01	0.15 ± 0.02 ***	0.14 ± 0.10 ***
GCI	0.03 ± 0.01	0.04 ± 0.01	0.03 ± 0.01

Results are expressed as mean ± standard deviation. (*): p<0.05; (**): p<0.001; (***): p<0.0001; NS (not significant) by Student's t-test. ED: distilled water; ZGD: Zigarda; GR: red blood cell; HB: hemoglobin; HT: hematocrit; VGM: mean corpuscular volume; TCMH: mean corpuscular hemoglobin; CCMH: mean corpuscular hemoglobin concentration; IRD: red blood cell distribution width; VPM: mean platelet volume; THT: Thrombocrit; P-LCC : White blood cell count; P-LCR: White cell ratio; IDP: Platelet distribution index; PLA: Platelet; GB: White blood cell; NEU: Neutrophil; LYM: Lymphocyte; MON: Monocyte; EOS: Eosinophil; BAS: Basophil.

Biochemical parameters

Zigarda was administered orally for 30 days at doses of 200 and 400 mg/kg to Balb/c

mice. The effects observed on biochemical parameters are presented in Table II.

Table II. Effects of Zigarda on biochemical parameters

Parameters	Lots		
	ED 0,1 ml/kg	ZGD 200 mg/kg	ZGD 400 mg/Kg
ALAT	29.45 ± 2.90	44.91 ± 6.60 **	37.33 ± 18.56
AST	43.99 ± 6.37	56.29 ± 7.22 *	57.45 ± 22.26 ***
GLY	0.10 ± 0.005	0.13 ± 0.04	0.13 ± 0.03
PROT	1.61 ± 0.40	1.74 ± 0.58	2.45 ± 0.58
CT	17.35 ± 4.70	30.78 ± 7.22 *	12.14 ± 1.40
HDL	36.49 ± 3.62	61.75 ± 31.20	49.40 ± 8.51 *
TG	64.12 ± 31.73	53.86 ± 24.97	31.88 ± 20.17

Results are expressed as mean ± standard deviation. (*): $p < 0.05$; (**): $p < 0.001$; (***): $p < 0.0001$; NS (not significant) according to Student's t-test. ED: Distilled water; ZGD: Zigarda; GLY: Blood glucose; TC: Total cholesterol; TG: Triglycerides.

DISCUSSION

Zigarda is a traditional recipe composed of three plants with numerous recognized therapeutic properties. Traditional medicine remains essential for more than 80% of the world's population⁹. This study aimed to evaluate the effects of the aqueous extract of the phytotherapeutic formulation Zigarda on hematological and biochemical parameters in Balb/c mice. An aqueous extract of the phytotherapeutic formulation Zigarda was prepared by cold maceration of 50 g of powder in 500 ml of distilled water for 72 hours, then evaporated using a Rotavapor. Eighteen Balb/c mice were divided into three groups: a control group treated with distilled water (0.1 ml/kg) and two groups (2 and 3) treated with Zigarda at doses of 200 and 400 mg/kg, respectively, for 30 days by oral administration. Hematological and biochemical parameters were analyzed after blood sampling.

Body weight changes were monitored to assess the effect of the treatments administered¹⁰. Zigarda was administered orally for 30 days at doses of 200 and 400 mg/kg to Balb/c mice. Figure (1) illustrates the body weight changes in Balb/c mice. Our results showed a gradual increase in weight in all groups. Group (2), treated with Zigarda at a dose of 200 mg/kg, had the highest weight values throughout the exposure period. Group (3), treated with Zigarda at a dose of 400 mg/kg, and showed a slight increase. The control group had a lower

increase compared to the groups treated with the therapeutic formulation. Prolonged administration of the aqueous extract of the therapeutic formulation Zigarda at the respective doses did not induce any apparent effect on the body weight change of Balb/c mice⁸.

Exposure to Zigarda at selected doses did not result in any deaths, adverse clinical signs, or toxic effects in animals throughout the administration period.

The complete blood count is a fundamental biological test that allows for the quantitative and qualitative analysis of blood cells¹¹. The phytotherapeutic formulation Zigarda was administered orally for 30 days at doses of 200 and 400 mg/kg to Balb/c mice. Table (I) shows the effects observed on hematological parameters. The results obtained from the groups treated with the phytotherapeutic formulation were compared with the group treated with distilled water as standards or reference values. Erythrocyte parameters are used to assess the condition of red blood cells and identify any abnormalities such as anemia or blood oxygenation disorders¹². Parameters related to the red blood cell line, including red blood cells, hemoglobin, hematocrit, and erythrocyte indices, showed a downward trend in Balb/c mice treated with the phytotherapeutic formulation. Our results showed a significant decrease in red blood cells ($p < 0.05$) and hematocrit ($p < 0.05$) with the phytotherapeutic formulation at a dose of 400 mg/kg, which may indicate moderate

anemia. Hemoglobin also decreased without reaching statistical significance. Mean corpuscular volume increased slightly at a dose of 200 mg/kg ($p < 0.05$), suggesting a tendency toward macrocytic anemia, while mean corpuscular hemoglobin concentration remained constant, indicating that hemoglobin concentration in red blood cells is stable despite their decrease in number. Platelet parameters provide information on platelet count, size, and functionality, which are essential for assessing hemostasis and the risk of bleeding or thrombosis¹³. They were particularly affected by the phytotherapeutic formulation. Our results showed a significant decrease in platelet count and thrombocrit, indicating possible thrombocytopenia for the group receiving the 400 mg/kg dose of the phytotherapeutic formulation Zigarda compared to the control group. In contrast, the mean platelet volume increased, suggesting increased production of young platelets. Our results showed changes in the P-LCR and P-LCC markers, indicating a non-linear dose-dependent effect on platelet size and distribution. Leukocyte parameters reflect the state and activity of the immune system, allowing the body's response to stimuli or treatments to be assessed^{14, 15, 16}. The results showed a highly significant increase ($p < 0.001$) in white blood cell count in the group receiving the 200 mg/kg dose and a highly significant increase ($p < 0.0001$) in the group receiving the 400 mg/kg dose of the aqueous extract of the phytotherapeutic formulation Zigarda compared to the control group. White blood cells defend the body against foreign agents. Their increase most often occurs during infection, but can also be caused by certain drugs and plants that stimulate the immune response^{17, 18, 19}. The significant increase ($p < 0.05$) in neutrophils for the group receiving the 200 mg/kg dose and the highly significant increase ($p < 0.0001$) for the group receiving the 400 mg/kg dose compared to the control group after administration of the phytotherapeutic formulation Zigarda probably reflected an immunostimulatory effect, resulting either from activation of bone marrow production

or increased mobilization of neutrophils in the blood^{16, 20, 21, 22}. The non-significant increase in lymphocyte levels for the group receiving the 200 mg/kg dose and the highly significant ($p < 0.0001$) increase for the group receiving the 400 mg/kg dose compared to the control group observed after administration of the phytotherapeutic formulation could suggest an immunostimulatory effect, reflecting activation of adaptive immunity through stimulation of lymphocyte proliferation and differentiation²³. The highly significant increase ($p < 0.0001$) in basophil counts observed after administration of the phytotherapeutic formulation Zigarda may reflect activation of the inflammatory component of the immune response, or a possible hypersensitivity reaction to the plant's active ingredients^{24, 25}. The highly significant increase ($p < 0.001$) in monocyte levels in the group receiving the 200 mg/kg dose, which was not significant in the group receiving the 400 mg/kg dose compared to the control group, observed after administration of the phytotherapeutic formulation could suggest stimulation of innate immunity, resulting from activation of bone marrow production and increased mobilization of monocytes involved in phagocytosis and the inflammatory response^{26, 27, 28}. The significant stimulation of different leukocyte lines after exposure to the phytotherapeutic formulation Zigarda may reflect an overall stimulation of the immune system^{17, 18, 29, 30, 31}. Our results may suggest an immunostimulatory effect acting on both innate and adaptive immunity, with a possible moderate inflammatory component. This response has a potential comparable to certain existing immunostimulants^{32, 33}. Biochemical parameters are essential indicators of organ function and integrity, allowing the assessment of metabolism, nutritional status, and the possible presence of toxicity or physiological dysfunction³⁴. The liver enzymes ALAT and AST, indicators of liver integrity, increased in the groups treated with the phytotherapeutic formulation Zigarda compared to the control

group after 30 days of administration. Blood sugar levels showed a slight, non-significant increase in the groups treated with the phytotherapeutic formulation Zigarda compared to the control group. Our results showed a gradual increase in plasma proteins in the groups treated with the phytotherapeutic formulation Zigarda compared to the control group. The phytotherapeutic formulation Zigarda had a biphasic effect on lipidemia. At a dose of 200 mg/kg, it increased total cholesterol and HDL. However, at a dose of 400 mg/kg, total cholesterol and triglycerides decreased, potentially indicating a lipid-lowering effect linked to the activation of lipid degradation pathways^{35, 36}. Our results suggest that the Zigarda phytotherapeutic formulation has interesting metabolic potential, particularly for lipid disorders, but with a potential hepatotoxic risk that needs to be monitored.

CONCLUSION

The herbal formulation Zigarda stimulates the immune system and improves certain lipid parameters, indicating an interesting immunostimulating and metabolic potential. Elevated liver enzymes underscore the need to define a safe therapeutic window. These properties may justify the exploration of the phytotherapeutic formulation as a source of new therapeutic strategies or immunostimulant supplements, subject to thorough studies.

Authors' Contributions

Participation in research design: AME Mbougou Malonga.

Experiments carried out: AME Mbougou Malonga, Alice Matété Mounoi, SM Osseke.

Contribution of new reagents or analytical tools: SM Osseke, A Matété Mounoi.

Data analysis performed: AME Mbougou Malonga, SM Osseke.

Authors or contributors to the manuscript: AME Mbougou Malonga, SM Osseke, Alice Matété Mounoi, LM Miguel, AA Abena.

Declaration by Authors

Ethical Approval: The study was conducted in compliance with Directive 2010/6106/EU on the protection of laboratory animals.

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Conflict of Interest: All authors declare that they have no conflicts of interest in relation to this work.

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