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HEMATOLOGICAL STUDIES ON THE EFFECT OF ZINGERONE ON STREPTOZOTOCIN INDUCED DIABETIC RATS.

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Abstract: Diabetes is a major metabolic disorder and by 2030, it would affect nearly 366 million populations worldwide, out of which 90% of the diabetic population would be insulin resistance. Such huge diabetic population would be a burden for any national healthcare system. Present study has been focused to evaluate the effect of zingerone on STZ induced diabetes mellitus. In the present study male Wister albino rats were used. The experiment was designed with 5 groups of animals, each group containing 6 animals. Group I served as control, group II rats were induced diabetes by the administration of single dose of STZ (40mg/kg body weight), group III rats were treated with zingerone (10mg/kg body weight) for 30 days after induction of diabetes group IV rats were treated with metformin (50mg/kg body weight) after the induction of diabetes & group V served as a zingerone (10mg/kg body weight) control. Hematological values are compared for normal to group II, III, IV. The result showed that WBC, RBC, HB, PCV, MCV, MCH, MCHC values are decreased in group II when compared to all other groups.

Keywords: Streptozotocin, Zingerone, Hematology, Diabetes

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INTRODUCTION

The World Health Organization (WHO) reported that 300 million people would suffer diabetes mellitus (DM) by the year 2025 (1). The disease is considered as important public health problem, especially in developing and 3rd world countries due to inadequate treatment (2).

Although herbal medicines have long been used effectively in treating many diseases throughout the world, the mechanisms of most of the herbs used have not been defined. Many traditional plant treatments for diabetes are also used, but most of the evidence for their beneficial effects is anecdotal (3). Ginger (*Zingiber officinale*) has been used as a spice for over 2000 years. Its root and the obtained extracts contain polyphenol compounds: 6-gingerol and its derivatives, which have high antioxidant activity (4) The medicinal properties of ginger were attributed to many active compounds in ginger. The major constituents in *Zingiber officinale* are the pungent vanilloids, gingerol, paradol, shogaols and zingerone (5). The antioxidant, antitumor, and anti-inflammatory pharmacologic effects of ginger were mainly attributed to these constituents (5).

The components of ginger might be helpful in combating the progression of various diseases such as oxidative stress, atherosclerosis, and diabetes mellitus among others (6). Further, there is no report on the antidiabetic effects of zingerone (4-(4-hydroxy-3-methoxy phenyl) butan-2-one), which is a stable active component of dry ginger rhizome and is known to have wide ranging pharmacological activities such as anti-oxidant (7) anti-inflammatory (8), antidiarrhoeal (9), antimicrobial (10), immunostimulant (11) and anticancer (12).

The present study is aimed to investigate the efficacy of zingerone in improving the hematological parameters in STZ-induced diabetic rats treated through oral administration of zingerone for 30 days.

Materials and methods

Chemicals

Zingerone and streptozotocin were purchased from Sigma-Aldrich, St Louis, MO.

Animals and Diet

Wistar albino male rats, weighing about 150-250 g, were obtained from King Institute of Preventive Medicine and Research, Chennai and maintained at animal house of Entomology Research Institute (ERI), Loyola College, Chennai. They were maintained under a constant 12 h light and dark cycle at 22–24 ^{o}C and at 45%-55% relative humidity in accordance with the guidelines of the National Institute of Nutrition, Indian Council of Medical Research, Hyderabad,

India. The study was approved by the Institutional Animal Ethical Committee (833/a/04/CPCSEA), Loyola College. Throughout the experimental period, the animals were fed with a balanced commercial pellet diet (protein, 21%; fat, 5%; nitrogen-free extract, 55%; fiber, 4%; adequate mineral and vitamin contents, 15%; Hindustan Lever Ltd., Mumbai, India) and water *ad libitum*.

Experimental Induction of Diabetes

Rats were induced diabetes with an intraperitoneal injection of STZ ((40 mg/kg bw) freshly prepared in 0.1 M sodium citrate buffer) after overnight fasting (13). The rats exhibited diabetes after 5 days (*i.e.*, fasting blood glucose concentration, >300 mg/dl) and were selected for the treatment with zingerone and with reference drug metformin separately.

Experimental Procedure

A total of 30 animals (6 normal and 24 diabetic rats) were used in the experiment. The rats were divided into the following 5 groups of 6 rats each: Normal control (Group I); Diabetic control (rats induced with STZ) (Group II); STZ-induced diabetic rats treated with zingerone (10 mg/kg bwt) orally for 30 days (Group III); STZ-induced diabetic rats treated with metformin (50 mg/b wt) orally for 30 days (Group IV); and Zio control (10mg/kg bwt) orally Zio only for 30 days (Group V) Animals were monitored for general health during the treatment period. No death of the animals was observed till the end of the study. At the end of the experimental period and after one day of last zingerone administration, the animals were deprived of food overnight and sacrificed by decapitation. Blood was collected and serum was separated for the estimation of insulin and other biochemical parameters.

Hematological parameters

The packed cell volume (PCV) was measured by the micro hematocrit centrifuge (14). Hemoglobin (Hb) concentration was determined by the cyano methemoglobin technique (15). The red blood cells (RBCs) and white blood cells (WBCs) counting methods were based on the dilution of obtained blood with diluting fluids (Hayem & Turke) in RBCs and WBCs counting pipettes (15). Individual cells were then counted in the counting chamber (hemocytometer). Giemsais staining method was used for the differential count of WBCs.

Statistical analysis

All data are given as mean ± SD (standard deviation). Statistical analysis was performed with past (version 3) several sample tests (ANOVA, kru - wal) followed by Tukey's pairwise test for multiple comparisons. Values of $p<0.05$ were considered significant.

Results

Table – 1 Comparative hematological values of G1-G5.Data are expressed as mean ± SD for six rats in each group. Values not sharing a common superscript letter (a-c) differ significantly at *P* < 0.05 (Tukey's pairwise test), NS-not significant. a-group I& II, b-group II& III, c-group II & IV ,d-group I & v

Parameters	G1	G2	G3	G4	G5
PCV (%)	41.53±0.15	35.66±1.79 [a]	38.33±1.24 [b]	37.5±0.95 [c]	40.98±0.24 d [NS]
Hb (g/dl)	12.46±0.34	11.81±0.19 [a]	12.05±0.27 [b]	12.19±0.29 [c]	12.44±0.12 d [NS]
RBCs ($\times 10^6 mm^3$)	6.41±0.13	5.04±0.23 [a]	6.83±0.15 [b]	6.04±0.10 [c]	6.38±0.19 d [NS]
MCV (μ^3)	63.48±0.24	69.27±0.25 [a]	64.41±0.13 [b]	65.16±1.06 [c]	63.09±0.17 d [NS]
MCH (Pg)	18.83±1.57	24.5±1.70 [a]	20.66±1.49 [b]	19.33±1.97 [c]	18.92±1.05 d [NS]
MCHC (%)	28.5±0.22	33.41±0.21 [a]	29.65±0.17 [b]	30.16±1.57 [c]	28.67±0.19 d [NS]
WBCs ($\times 10^3/mm^3$)	8.98±0.15	7.48±1.09 [a]	8.31±0.03 [b]	8.46±0.12 [c]	8.85±0.23 d [NS]

PCV = packed cell volume; Hb = hemoglobin; RBC = red blood cell count; WBC = white blood cell count; MCV = mean corpuscular volume, MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration.

DISCUSSION

Referring to Table 1 in the present study, which indicated that treatment with Zingerone might ameliorate some disturbed hematological parameters of diabetic rats, it has been suggested that anemia occurrence in DM is due to the increased non-enzymatic glycosylation of RBC membrane proteins, which correlates with hyperglycemia (27). Oxidation of these glycosylated membrane proteins and hyperglycemia in DM caused an increase in the production of lipid peroxides causing hemolysis of RBC. Hematological indices are indicators and reflection of the effects of dietary treatments on animals in terms of the quality of feed ingested and nutrients available to the animal to meet its physiological requirements. The values of hemoglobin (Hb), an iron-containing conjugated protein that performs the physiological function of transporting oxygen and carbon dioxide, which did not show any significant changes in diabetic or diabetic treated groups compared with those on the control diet group, suggest that the animals did not suffered depressed respiratory capability at any group indicating that the oxygen-carrying capacity of the blood of the animals are not affected either in diabetic or diabetic treated

groups. Thus, increased RBC count of Zingerone treated diabetic rats could be due to the lowered lipid peroxide level in RBC membrane leading to a decreased susceptibility of RBC to hemolysis. Since non-enzymatic glycosylation of membrane proteins correlate with hyperglycemia (16), it might be said that Zingerone produced their effect by decreasing the elevated glucose concentration in treated diabetic rats. Therefore, our results suggest that the Zingerone stimulate the synthesis (erythropoiesis) and concentration of erythrocytes till normalizing RBC in anemic diabetic rats. The corresponding statistical decrease in the PCV (measure of the volume of blood consisting of solid cells) of the diabetic animals and its normalizing with Zingerone treatment suggest their role in erythropoiesis. Taken together, the results of RBC, Hb and PCV suggest that the Zingerone possess antioxidant properties and help in RBC membrane stabilization by binding to proteins and carbohydrates which are components of RBC membrane and therefore may prevent breakdown of RBC membrane and antagonize the anemic effect of Streptozotocin. Neutrophils ingest and kill bacteria and have been called the body's first line of defense against bacterial infections (17). It has been suggested that the body's defense mechanism against infections was disturbed due to the disturbed neutrophil function in diabetes (18). In this experiment, we demonstrated that treatment of diabetic rats with Zingerone increased the lowered neutrophil percentage of WBC to the control level. This result indicated that Zingerone treatment might also increase the defense mechanism of the body against infections in diabetic rats. As mentioned above, it was found that RBC count increased to control level in Zingerone treated diabetic rats. Therefore, return of blood indices (MCV, MCH, MCHC) in diabetic treated rats could be due to a normalized RBC count in these rats. From the hematological results, it is apparent that oral administration of Zingerone might decrease the diabetes-induced disturbances of hematological parameters in STZ-induced diabetic rats. Data of the present study revealed that daily treatment with Zingerone markedly improves hematological statuses of rats with STZ-induced diabetes.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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