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Guardians of Liver Health: Unveiling the Resilient Shield of Antioxidant Vitamins (C, E) Against Glyphosate-Induced Havoc in Experimental Rats

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Abstract

Glyphosate, a widely used herbicide, has gained popularity due to its broad-spectrum effects and use in genetically modified, glyphosate-resistant crops. Recent data, however, points to possible adverse effects of glyphosate and herbicides based on glyphosate, such as genotoxic and cytotoxic effects, elevated stress levels, disturbance of the hormones such as estrogen pathway and possible associations with specific cancer types. This has raised concerns about the widespread use of glyphosate and its impact on human health and the environment. The objective of this study was to determine whether antioxidants vitamin C and E could shield experimental rats' livers from the damaging effects of glyphosate. Animals were grouped as Group I-control, 30 days of oral glyphosate-treated rats as Group II, and Rats that received simultaneous glyphosate treatment and oral administration of vitamins C and E were for 30 days as Group III. We used the user's manual to figure out the fasting blood glucose (FBG) levels, the histomorphology of liver tissue using H&E staining, and the liver and kidney function tests using Diatek Greiner kits. The study revealed that prolonged exposure to glyphosate can alter the SREBPI and HNF1 pathways, leading to diabetes. As an herbicide, glyphosate can cause harmful changes in vital organs, leading to diabetes and other disorders.

Keywords: *Glyphosate, Vitamin C and E, and Diabetes.*

Introduction

Herbicides like glyphosate are widely utilized all over the world. As a broad-spectrum herbicide, glyphosate became more popular in agriculture after the development of genetically modified varieties that are resistant to it. Recent research suggests that glyphosate and herbicides based on glyphosate can cause damage to cells and genes, increase the level of oxidative stress, disrupt the estrogen pathway, hinder cognitive functions, and may be linked to certain forms of cancer [1]. The use of glyphosate has increased in recent years, causing concern over its potential toxicity and impact on human health. However, there is currently no agreement within the scientific community, and the safety and health effects of glyphosate remain a topic of controversy [2].

Concerns have been raised about the potential impact of glyphosate on human health, given that this herbicide is mainly used in fields and can persist for several months in the soil. Therefore, this study aims to review the

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use, toxicity, and occurrence of glyphosate in various food samples, some of which contain higher-than-allowed levels. To date, 32 countries have banned the use of glyphosate. Public health awareness has increased as a result of the presence of glyphosate in food at levels above the legal limit and the substance's alleged toxic effects [3].

Oxidative stress is a condition where the balance between prooxidants and antioxidants is disrupted in favour of the former, leading to potential harm. There is an increase in ROS, or reactive oxygen species, and a weaker antioxidant defence mechanism, or the ability to repair oxidative damage is reduced, causing this condition. Proteins, DNA, and membrane lipids are examples of biological macromolecules that can sustain damage from ROS [4]. Damage-induced variations in intracellular calcium levels or pH can alter cell function and ultimately result in cell death.

The cellular defence system typically controls the overproduction of free radicals and the resulting harm to cells and tissues [5]. Both enzymatic and non-enzymatic mechanisms, such as vitamins and glutathione, support this preventative defensive system. Antioxidant enzymes like GPx, GST, GR, CAT, and SOD may be very important in lowering the harmful effects of ROS.

Recent research indicates that the increased generation of ROS may explain the various forms of toxic reactions caused by pesticides. Studies have proven that there is a connection between the production of ROS and toxic manifestations. There has been speculation that xenobiotics and pathological conditions can cause oxidative stress, which generates ROS and causes various types of tissue damage. According to numerous studies, the toxicity of organochlorine, organophosphate, and pyrethroid insecticides has been connected to ROS. Furthermore, experiments have revealed that the majority of environmental pollutants, such as polychlorinated biphenyls (PCBs) and bisphenol A, induce stress oxidatively in the rat’s kidney, liver, and lungs.

Antioxidants such as vitamins E and C are capable of halting, the uncontrolled creation of free radicals or hindering their interaction with biological sites. Additionally, endogenous antioxidants need to be oxidized, which largely involves scavenging and reducing molecules, to eliminate most free radicals. Research indicates that the water-soluble antioxidants, vitamins C and E, can prevent genetic mutations by disposing of ROS and impairing oxidative DNA [6].

This study aims to analyze the protective effect of vitamins C and E against the harmful effects of glyphosate on the liver of experimental rats. The goal is to find out how vitamins C and E protect the livers of rats that were exposed to glyphosate.

Materials and Methods

To ensure adherence to ethical research practices, approval was obtained from the Institutional Animal Ethical Committee (IAEC) under the registration number BRUL. Evaluation encompassed fasting blood glucose levels and histomorphological assessments. Liver and renal function tests were conducted, employing SGOT and SGPT for liver function, and Diatek and Greiner kits for renal function, estimating Creatinine, Urea, and Uric Acid levels.

Animals

The study involved adult male Albino Wistar rats weighing between 150 and 180 g. The Institutional Animal Ethical Committee (IAEC) granted ethical approval for the animal-related experimental protocols under the registration number BRULAC/SDCH/SIMATS/IAEC/8-2021/086. The rats were maintained in a controlled environment.

Experimental Design

The experimental design involved the allocation of six healthy male albino rats to each of the three groups. The control group received intraperitoneal injections of corn oil once daily. The second group was orally administered glyphosate for 30 days, and the third group received Aroclor 1254 + vitamin E and vitamin C simultaneously for the same duration.

Post-treatment, the animals underwent anaesthesia with ether, blood collection, and serum storage at -80°C. Dissected liver samples from both the treated and untreated animals were evaluated using a variety of parameters.

Fasting Blood Glucose (FBG)

Fasting blood glucose (FBG) levels were determined.

Histology and Biochemical Analysis

Histological evaluation of liver tissue was performed using H&E staining. Biochemical analyses for liver function (SGOT, SGPT) and renal function (creatinine, urea, and Uric acid) were conducted according to user manual instructions, utilizing Diatek and Greiner kits.

Results

The levels of FBG, serum insulin, SREBP-1c, and HNF-1 are depicted in Figure 1. One-way ANOVA (Figure 2) comparing the control and other groups showed no significant p-value of 0.05 and a difference of comparison (dof) of 4. However, it is clear from the study that the glyphosate group could shield rats from glyphosate-induced hepatic stress when given vitamins C and E. The results showed that when vitamins C and E were given together, fasting blood sugar levels were lowered, serum insulin levels were increased, lipogenic processes were altered, and hepatocyte nuclear function was improved in comparison to the group that was exposed to glyphosate without the vitamins.

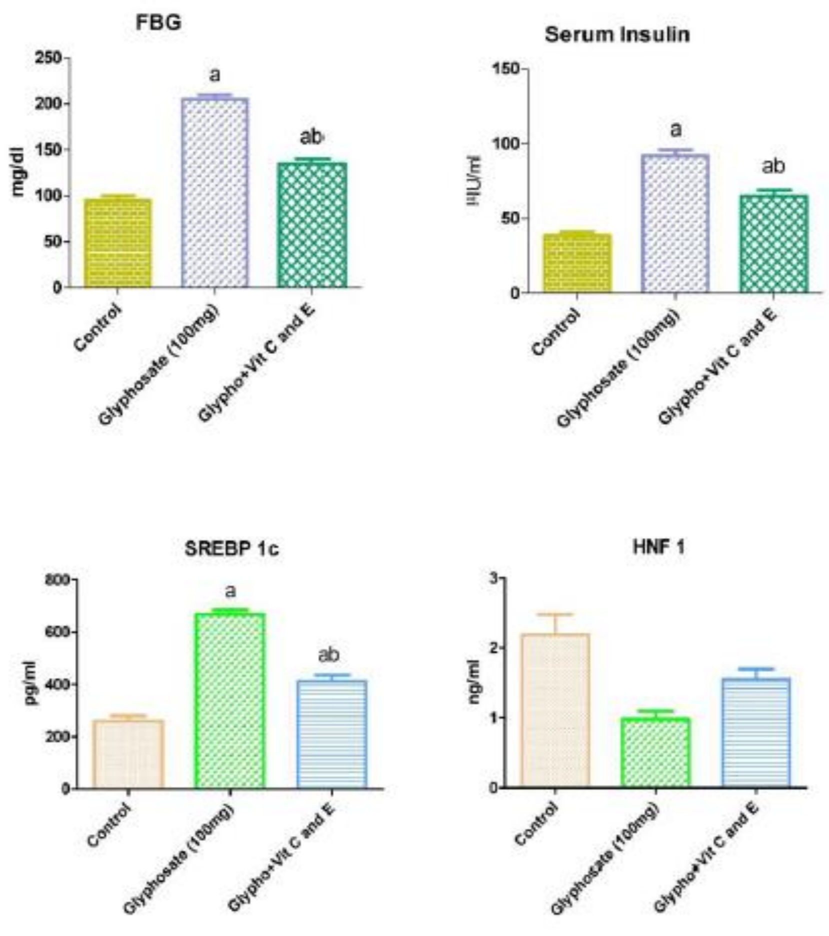

Figure 1. The Levels of FBG, Serum Insulin, SREBP-1c, and HNF-1 Among Control, Glyphosate and Glyphosate + Vitamin C and E

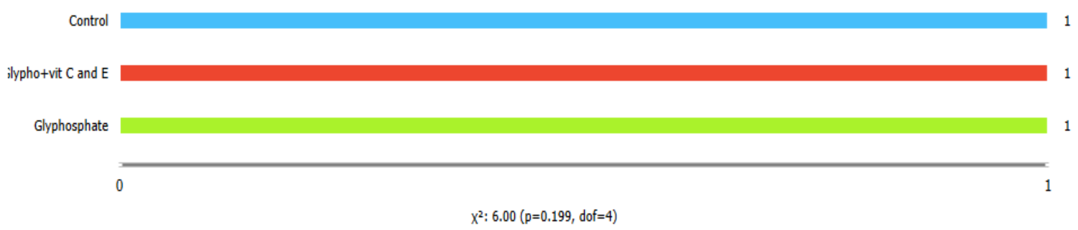

Figure 2. One-way Anova Showing Comparing Among Groups with Significance of $p < 0.05$

Discussion

The rats that were not treated with glyphosate had normal fasting blood glucose levels, indicating that they were able to regulate their blood sugar levels effectively. However, rats that were treated with glyphosate exhibited elevated levels of fasting blood glucose, suggesting that the herbicide disrupted their ability to regulate blood sugar [7]. Interestingly, when glyphosate was combined with Vitamin C&E, the levels of fasting blood glucose were still elevated, but not as much as in rats that were treated with glyphosate alone. The result shows the protective effect that vitamins C and E had, which lessened the detrimental effects of glyphosate on blood sugar management [8]. The study also discovered that rats given glyphosate had higher serum insulin levels. Serum insulin is a hormone that controls blood sugar by encouraging the absorption of glucose into cells. However, when glyphosate was combined with Vitamin C&E, the levels of serum insulin were still elevated, but not as much as in rats that were treated with glyphosate alone. Once again, this is because Vitamin C&E provided a shielding effect that helped to reduce the negative impact of glyphosate on insulin regulation [9]. Overall, this study highlights the potential risks associated with glyphosate exposure and the importance of exploring ways to mitigate its negative effects on blood sugar and insulin regulation [10].

People who have type 2 diabetes and obesity have significantly higher levels of the transcription factor SREBP1c. This type of protein plays a role in insulin resistance and is a major factor in the buildup of fats in the liver. Recent studies have revealed that rats treated with glyphosate, a widely used herbicide, have shown an increase in SREBP1c levels [11]. This increase in SREBP1c level could potentially lead to the development of diabetes and related complications. These findings suggest that glyphosate exposure may be a contributing factor to the rising rates of diabetes and metabolic disease in modern populations [12].

The study found that animals treated with both glyphosate and vitamin C&E showed a slight increase in SREBPIc, [13] a protein that

effects plays a major role in regulating the metabolism of lipids and cholesterol [14].

However, this increase was not as significant as that observed in the animals treated with glyphosate alone. This suggests that vitamin C&E may have some antioxidant properties that could help mitigate the harmful effects of glyphosate on the body. Additionally, the study found that type 2 diabetes is caused by a mutation in the HNFI gene [15, 16]. HNF I, a transcription factor that controls the transcription of genes involved in glucose metabolism, was dramatically reduced in the rats treated with glyphosate. Recent studies have delved into diverse aspects of research [17, 18 ,19]

On the other hand, the levels of HNF I were higher in the control group and the group that received both glyphosate and vitamin C&E [20 ,21]. This shows that vitamin C and E may protect against glyphosate's detrimental on glucose metabolism, although further studies are required to validate this.

Conclusion

Glyphosate, when used as an herbicide, has the potential to cause harmful changes in vital organs, and may also lead to the development of diabetes and other disorders.

It is a known fact that every antidiabetic drug comes with its own set of side effects. Therefore, it is recommended to opt for homoeopathic medicine instead of allopathic medicine, as it can help reduce the side effects caused by them.

In light of the above evidence, we can infer that the antioxidant vitamins E and C possess protective effects. According to the study, regular consumption of vitamins E and C can help protect against diabetes.

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Conflict of Interest

The authors hereby declare that there is no conflict of interest in this study.

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