



SUB-CHRONIC TOXICITY STUDIES OF QUIZALOFOP-P-ETHYL IN FEMALE WISTAR ALBINO RATS

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ABSTRACT

Quizalofop-p-ethyl marketed as Targa Super is widely used effective herbicide. An attempt has been made to assess the toxic effect of Quizalofop-p-ethyl, rats were given oral doses of 1/25 of LD50 of the Quizalofop-p-ethyl (59.2 mg/kg of body weight) dissolved in water for 120 days. Haematological analysis shows significant increase in TLC, particularly neutrophil ($51.67^{**\pm} 11.25$), lymphocyte ($44.17^{**\pm} 11.58$) and eosinophil ($2.5^{**\pm} 1.2247$), whereas no any observable changes were found in Hb % and RBC. Where, the biochemical analysis shows significant increase in protein ($9.3^{**\pm} 0.68$), a slight increase in the alkaline phosphatase, cholesterol and potassium, while no variations in the glucose and electrolytes were recorded. A significant increase in the relative weight of lung ($1.229^{**\pm} 0.057609$) with a slight increase in weight of the liver and significant decrease in weight of the ovary ($0.0515^{**\pm} 0.0014$) was observed. It has been also observed that Qzalofop-p-ethyl induced swelling on intestine and liver. Symptomatic behavioral changes were also observed. Comparing the toxicity of Quizalofop-p-ethyl widespread use of this herbicide in public places is to be prohibited or restricted.

Keywords: Quizalofop-p-ethyl, Haematological, Biochemical analysis.

INTRODUCTION

Herbicides include a variety of chemical compounds used to control and eliminate weeds and pests in both agricultural and non-agricultural settings. They are also used to control weeds in forests, pastures, parks,

athletic fields, golf courses, ponds, lakes and home lawns and gardens. But the uncontrolled and excessive use of herbicides leads to various hazardous effects. High concentration of herbicide normally occurs in the environment for a short period after their accident [1].

Quizalofop-p-ethyl marketed by trade name 'Targa Super' in Maharashtra, other trade name are Assure II, Pilot super, Matador, Leopard [2]. It is a selective, post-emergence phenoxy herbicide [3]. Quizalofop-p-ethyl should not be confused with the Quizalofop or Quizalofop ethyl. The latter two compounds are distinctly different than former one. It is used to control annual and perennial grass weeds in potatoes, soybeans, sugar beets, peanuts, vegetables, cotton and flax, as well as other crop [2]. Quizalofop-p-ethyl is moderately persistent in soil, with a reported half-life of 60 days [4]. It is absorbed from the leaf surface and transferred throughout the plant, moving in the xylem and phloem and accumulates in the meristematic tissue. It accumulates in the active growing regions of the stem and roots [2]. The indiscriminate use of herbicide in agriculture, as well as the increase of pollution in ecosystem due to the industrial development, justifies the evolution of toxicity of these chemicals [5]. There is dearth of literature on Quizalofop-p-ethyl toxicity.

The purpose of this study was to investigate the effect of Quizalofop-p-ethyl on the haematological and biochemical parameters of female Wistar rats. As with the recurrence of weeds, repeated use of herbicide is very common, the lower dose of Quizalofop-p-ethyl (1/25 of LD 50) is used to experiment on the assumption that such



dose could be contained in food of plant origin that had been treated with the concentrations recommended by the manufacturer of these herbicides.

MATERIAL AND METHODS

Herbicide: Chemical name of Quizalofop-p-ethyl is (R)-2-[4-(6-chloroquinoxalin-2-yloxy) phenoxy] propionic acid, marketed by trade name 'Targa Super' in Maharashtra, other trade name are Matador, Assure II, Pilot super, Leopard, etc.

Animal material: Healthy female albino Wistar rats (150 ± 5gm) were procured from Sudhakar Rao Naik College, Pusad. These animals were maintained on a standard diet and water provided *ad libitum*. The animals were divided in two groups. Group 'A' served as control and consists of six rats. Group 'B' was experimental and consists of six rats. Each experimental rat was given an oral dose 1/25 of LD 50 value (59.2 mg/kg of body weight) of Quizalofop-p-ethyl dissolved in 1ml normal tap water for 120 days, whereas each rat in the control group 'A' was given an equal amount of normal tap water by the same route. The rats of group 'A' were sacrificed on the 120th day while group 'B' rats were dissected on the 121st day after giving 120 days oral dose according to the norms of ethical committee (1060/ac/07/CPCSEA). Blood was collected for haematological and biochemical estimation from the renal artery.

Methods for Haematological and Biochemical analysis:

The Haematological and Biochemical tests were conducted at Dr. Panjabrao Alise Bhausaheb Deshmukh Medical College, Amravati using Beckman counter machine, CBC counter machine and Neubar counting chamber for Haematological analysis while Biochemical

analysis was performed with help of by fully automatic analyzers biochemical analyzer "selectra -E".

Statistical analysis

Students t-test was used to compare the data. The difference was calculated statistically significant if the $p^* < 0.05$, and $p^{**} < 0.01$

RESULTS

Rats were exposed daily to Quizalofop-p-ethyl (dissolved in tap water) at the dose level of 1/25 of the LD 50 value i.e. 59.2 mg/kg of body weight for 120 days. There was a weight gain in experimental rats during the first few weeks (5-6 weeks) of study, but in the latter period weight loss was observed while a weight of control rats remains constant.

Experimental rats showed lethargy, red nose and eye discharge and decreased food intake, Sneezing and difficulty in breathing. Stomach was observed filled with fluid having pungent smell. Ulceration and inflammation of intestine, tumor like growth/lesions on liver was also observed in all most all experimental rats.

Lung and ovary show significant changes in their weight. The weight of the lungs ($1.229^{**} \pm 0.057609$) increased significantly, whereas ovarian weight ($0.0515^{**} \pm 0.0014$) decreased significantly [Table 1].

Quizalofop-p-ethyl administration in the rat caused significant increase in TLC, particularly neutrophil ($51.67^{**} \pm 11.25$), lymphocyte ($44.17^{**} \pm 11.58$) and eosinophil ($2.5^{**} \pm 1.2247$) whereas no any observable changes are found in haemoglobin % and RBC. [Table 2].

Biochemical analysis shows significant increase in total proteins ($9.3^{**} \pm 0.68$). Slight increase in the alkaline phosphatase, cholesterol and potassium, [Table 3] while no variations in the glucose and electrolyte was found.

Table 1. Effects of oral administration of Quizalofop-p-ethyl on relative organ weight of Wistar female rats

Parameters	Control	Quizalofop-p-ethyl
Lung	1.042±0.211206	1.229**±0.057609
Thyroid	0.2477±0.2757	0.146±0.014156
Ovary	0.0768±0.007548	0.0515**±0.0014
Liver	6.3475±1.364287	7.30±0.8

Table 2. Haematological profile, effect of Quizalofop-p-ethyl on rats (n=6)

Parameters	Control	Quizalofop-p-ethyl
Hb%	11.16±2.12	12.5±0.86
R.B.C. Millions /cu mm	6.13±0.686	6.19±0.270
T.L.C. thousand/cumm	6350±1338.28	6583.3**±2375.219
Neutrophil %	18.83±6.24	51.67**±11.25
lymphocyte%	77.33±5.78	44.17**±11.58
Eosinophil%	1±0.63	2.5**±1.2247
Monocyte%	2.8±1.32	1.67±0.816497



Table 3. Biochemical profile, effect of Quizalofop-p-ethyl on rats (n=6)

Parameters	Control	Quizalofop-p-ethyl
Glucose (mg/dl)	149.33±64.83	151±64.95
Serum alkaline phosphatase (U/l)	381±252.22	429.67±286.9
Proteins(gm/dl)	8.115±1.618	9.3**±0.68
Serum cholesterol (mg/100ml)	54±17.66	58.33±21.537
Sodium(mEq/l)	140.8±4.355	149.67±5.08
Potassium(mEq/l)	6.05±1.68	9.83±1.546178
Calcium(mgm/dl)	5.3±0.42	5.8467±0.856847

Values are given as mean of six separated animals ± standards deviations.* $p < 0.05$; ** $p < 0.01$ (Student's t-test).

DISCUSSION AND CONCLUSION

Herbicides are used in vegetables and crops to increase the yield or to protect them from any hazard or injury. However researchers found that if the amount of herbicides spray exceed than recommended amount it affects soil, field workers and consumers also. These herbicides can causes adverse effects and can leads to several hazardous diseases.

The Quizalofop-p-ethyl is selective, post-emergent, phenoxy herbicides, used to control annual and perennial grass weeds in potato, soybeans, sugerbeats, peanuts vegetables etc. [3].

In the present study Quizalofop-p-ethyl treated rats show decrease in body weight, lethargy, red nasal and eye discharge and decreased food intake. Sneezing and difficulty in breathing was also observed. Stomach was observed filled with fluid having pungent smell. Ulceration and inflammation of intestine, edema/lesions of liver was also observed in all most all experimental rats. Similar findings were observed by SUN Jian-xi, the decrease in food consumption, body weight, food efficiency and the increase in the organ coefficients of brain, heart, lung, liver, kidney on sub-chronic exposure to Quizalofop-p-ethyl [7].

A slight increase in the liver weight was observed [Table 1]. Quizalofop-p-ethyl, an often applied herbicide, is a probable inducer of occupational liver injury, according to the World Health organization [8]. Increased liver weights and some changes in liver tissue structure were detected in an 18-month carcinogenicity study on mice [4]. Study in mice with diets that contained 0, 100, 316, or 1,000 ppm (approximately 0, 15, 47.4, and 150 mg/kg/ day, respectively), of Quizalofop-p-ethyl, the no observed effect level (NOEL) was < 15 mg/kg/day (the lowest dose tested) shows increased liver weight and reversible histopathologic effects in the liver like centrilobular and generalized hepatocyte enlargement and eosinophilic changes in animals livers [10].

Lung and ovary show significant changes in their weight. The weight of the lungs ($1.229^{**} \pm 0.057609$) increased significantly, whereas ovarian weight ($0.0515^{**} \pm 0.0014$) decreased significantly [Table 1]. According to the EXTONET, because of the low viscosity

of this product, it may directly enter the lungs if swallowed, or if subsequently vomited. Once in the lungs, it is very difficult to remove and can cause severe injury or death. However, this product may be irritating to mucous membranes, but is unlikely to cause anything more than transient discomfort [3].

Quizalofop-p-ethyl administration in the rat caused significant increase in TLC, particularly neutrophils ($51.67^{**} \pm 11.25$), lymphocytes ($44.17^{**} \pm 11.58$) and eosinophils ($2.5^{**} \pm 1.2247$) whereas no any observable changes were found in haemoglobin % and RBC. [Table 2]. The similar results were observed by Kobal and Budihna for phenoxy herbicide 2,4-D, a sub-acute toxicity test using 2, 4-dichlorophenoxyacetic acid (2, 4-D, 10 mg/kg/l & 100mg/kg/l) and 4-chloro-2-methylphenoxyacetic acid (MCPA, 15 mg/kg/l & 150 mg/kg/l) was carried out on Wistar rats (n = 60) and New Zealand White rabbits (n = 30) of both sexes. The administration of herbicides 2, 4-D or MCPA did not significantly affect the red counts neither in rats nor in rabbits, as compared to controls. However, there were great differences in leukocyte counts within all groups [11].

Biochemical analysis shows significant increase in total proteins ($9.3^{**} \pm 0.68$). Slight increase in the alkaline phosphatase, cholesterol and potassium, [Table 3] the pesticides exposure resulted in to the dose dependent increase in the protein, stress increases the physiological activity which in turn will demands in mobilization of proteins to meet the energy required to overcome this stress, there may be increase in protein synthesis [6]. An increased serum Alkaline Phosphatase may be due to congestion or obstruction of the biliary in the liver, while no variations in the glucose and electrolyte was found.

Oral treatment of Quizalofop-p-ethyl at dose of 1/25 of LD 50 in female albino Wistar rats produced significant harmful effects on some of the haematological and biochemical parameters. Quizalofop-p-ethyl is found to be harmful if swallowed, if aspirated may cause lung damage, so avoid recurrence in order to minimize risks to persons using the product in the workplaces. Also, avoid contact or contamination of product with incompatible materials.



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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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