Advances in Bioresearch
Adv. Biores., Vol 8 (5) September 2017: 102-112

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.8.5.102112

Advances in Bioresearch

ORIGINAL ARTICLE

Alteration in Physiological and Haematological profile of female albino wistar rats over 90 days oral repeated exposure by Fomesafen

Alok Paliwal[1], ML Agarwal[1], KM Chacko[1], Anurag Singh[2], Abhishek Chauhan, Tanu Jindal[3*]
[1]Shriram Institute for Industrial Research, 19-University Road, Delhi-110007, India
[2]EM Facility, Department of Anatomy, AIIMS, Delhi-110029, India
[3] Amity Institute of Environmental Toxicology, Safety and Management,
Amity University, Sector-125, Noida, Uttar Pradesh, India
Email: tjindal@amity.edu

ABSTRACT
The present study deals with the evaluation and assessment of the safety/toxic potential of Fomesafen , a well known herbicide from diphenylethern group group used for the weed management of broad-leaved weeds in Legumes; Cotton; Soybeans; Potatoes; Tomatoes etc. using physiological and hematological parameter in albino wistar rats. A repeated dose oral (90 days) toxicity study of Fomesafen technical was carried out. For this,10 female albino wistar rats of were treated with Fomesafen technical them at three different doses i.e. 50, 100 and 250 mg/kg B. wt. /day. As a control, 10 female albino wistar rats were treated with corn oil only which was the vehicle. Two groups consisting of 10 female rats were kept as control recovery and Intermediate dose recovery group which were treated with the vehicle (corn oil) and Fomesafen technical at the dose of 100 mg/kg B. wt. Animals of control recovery (corn oil) and Intermediate dose recovery groups (100 mg/kg B.wt.) were further observed for 28 days without any treatment. From this study, it was found that the rats treated with high dose (250 mg/kg B. wt.) of the Fomesafen technical gained their body weight with less rate than that of the control group (corn oil). However, The haematological parameters of all the dose group animals were comparable to the parameters of control group animals, when evaluated at 0 day, 45th day and at terminal sacrifice. Similarly, the parameters of recovery intermediate dose group (100 mg/kg B.wt.) animals were comparable to their Recovery control counter parts as the parameters fell within the accepted laboratory limits.
keywords: Fomesafen, haematological parameters

Received 15/04/2017 Revised 09/06/2017 Accepted 01/08/2017

How to cite this article:
A Paliwal, ML Agarwal, KM Chacko, A Singh, A Chauhan, T Jindal. Alteration in Physiological and Haematological profile of female albino wistar rats over 90 days oral repeated exposure by Fomesafen. Adv. Biores., Vol 8 [5] September 2017: 102-112.

INTRODUCTION

India is the world's second largest producer of rice, wheat and cotton after China; and the second largest producer of sugarcane, after Brazil. It is also the second largest global producer of horticultural products. Moreover, India is the world's second largest importer of vegetable oils besides being the largest producer, consumer and importer of pulses (grain legumes). However, productivity of these crops is far lower than that of developed countries and China. To meet the demands of an increasing population and avoid food imports, crop productivity in India needs major improvements, which can be attained by identifying the constraints that hinder fanners in achieving high yields.

In India, weeds are one of the major biological constraints that limit crop productivity. They compete with crops for natural and applied resources besides being responsible for reducing quantity and quality of agricultural productivity [1,2], despite continuous research and extension efforts made. Bhan et al. [3] estimated that weeds in India reduce crop yields by 31.5% (22.7% in winter and 36.5% in summer and kharif seasons). In other studies, weeds were reported to cause up to one-third of the total losses in yield, besides impairing quality of produce and causing health and environmental hazards [4]. In a survey,

Indian weed scientists estimated losses due to weeds from 10% to 100% (Table 2). Even a conservative estimate of about 10% loss [3] would amount to a loss of food grains valued at approximately US$ 13 billion [5]. Losses of this magnitude due to weeds may occur in plantation crops, fruits, vegetables, grasslands, forestry and aquatic environments. The total economic losses will be much higher, if indirect effects of weeds on health, losses of biodiversity, nutrient depletion, grain quality, etc. are taken into consideration.

To counter this problem, effective weed management is require in order to do so the use of herbicides is increasing in worldwide crop production. The value of the worldwide herbicide market grew by 39% between 2002 and 2011 and is projected to grow by another 11% by 2016 [6]. Herbicides are being rapidly adopted in developing countries that face shortages of hand weeding labor and the need to raise crop yields [7]. Improved weed control with herbicides has the potential greatly to improve crop yields in many developing countries in the near future [8]. Increased herbicide use promotes fertilizer use, which leads to even greater yield increases [9]. But the increases usage of herbicide must also be done only after the toxicity assessment and safety evaluation of these herbicides. Therefore, the present study is designed to evaluate the effect of Fomesafen technical on Physiological & hematological parameter of female albino wistar rats over a repeated oral exposure for 90 days. Fomesafen is a herbicide of diphenylether group and is effective against the of broad-leaved weeds in crops like Legumes; Cotton; Soybeans; Potatoes; Tomatoes etc. Fomesafen act by Inhibition of protoporphyrinogenoxidase (PROTOX) enzyme. PROTOX is an important enzyme involved in chlorophyll and heme biosynthesis; its inhibition leads to a chain of reactions that ultimately results in lipid peroxidation; lipids and proteins are attacked and oxidized, resulting in loss of chlorophyll and carotenoids and in leaky membranes which allows cells and cell organelles to dry and disintegrate rapidly. Fomesafen get activated by exposure to sunlight to form oxygen compounds such as hydrogen peroxide. These oxygen compounds destroy plant tissue by rupturing plant cell membranes. Destruction of cell membranes results in a rapid browning (necrosis) of plant tissue. As Fomesafen is a contact herbicide, it is excellent for burndown of existing foliage and control of annual weeds.

MATERIAL AND METHOD

Test substance

Fomesafen technical was provided by one of Indea's leading agrochemical manufacturer. It was in the form of powder. The test substance was soluble in corn oil which served the role of vehicle for the dosing. The purity analysis of Fomesafen technical was checked by HPLC method using C-18 coloumn, Mobile phase in ratio of 40:60 (water: ACN), flow rate: 1 ml/min. Wavelength: 290 nm, Temperature: 35^0C. The concentrations in the doses formulation were determined by HPLC method showing 100 % homogeneity in the solution.

Animals and their treatment

Rats used for the study were bred at the animal house facility of Shriram Institute for Industrial Research, Delhi. For the study, 5 to 8 weeks old female wistar rats weighing between 100 to 140 grams were used. Prior to starting the experiment, necessary approvals were taken from IAEC (Institutional animal ethics committee) and CPCSEA (Committee for the Purpose of Control and Supervision of Experimental Animals) for conducting the study. The animals were housed (3 rats each cage) in an air conditioned room (12-15 air changes per hour) at the temperature 22 ± 3 °C and 30-70 % relative humidity with a 12 hour light/ dark cycle. They were provided with standard laboratory animal diet (Amrut feed Ltd) and filtered water ad-libitum. The animals were acclimatized for five days prior to the initiation of experiment. The various group of experimental animals used in the study are summarized in Table 1.

Table 1: ANIMAL GROUP AND DOSAGE LEVELS FOR MAIN STUDY

Group	Dosage Level (mg/kg B.wt.)	Animals used	Terminal Sacrifice (Sacrificed after 90 days dose administration)	Post Terminal Sacrifice (Sacrificed after 28 days post treatment)
Control (vehicle only)- **G1**	0	10	10	-
Low dose- **G2**	50	10	10	-
Intermediate dose- **G3**	100	10	10	-
High dose- **G4**	250	10	10	-
Recovery Control- **G5**	0	10	0	10
Recovery Intermediate Dose- **G6**	100	10	0	10

Parameters studied

All experimental animals were examined, once daily, for clinical signs, symptoms and for mortality. Detailed clinical observations (eye abnormalities and apparent functional changes) were made for each animal once before the start of dose administration and thereafter weekly till termination of the study. Body weight of each animal was recorded before initiation (Day zero) and weekly thereafter up to the termination of the study. Body weight of each of the fasted animals was taken, to calculate the organ weight ratio just before their sacrifice. At pretest (Day zero), interim (45 days), the end of the treatment (91 day) and of the recovery period (119 days), all animals were kept for fasting overnight before collecting their blood for Hematology examination. Blood samples were collected via orbital sinus under light CO_2 anesthesia. Following Hematology parameters were determined by using Beckman Coulter hematology analyzer.

Hb : Hemoglobin (g%) RBC : Red Blood Corpuscles (x 106 /cmm)
HCT : Hematocrit (%) Platelets (x 105 /uL)
Reticulocytes (%) WBC : White Blood Corpuscles (x 103 /uL)
Prothrombin Time (in seconds)
Analysis of the following (Differential leucocyte counts) parameters were performed manually:
N: Neutrophils (%) B: Basophil (%)
L: Lymphocytes (%) E: Eosinophils (%) M: Monocytes (%)
% Body weight gain:
The percentage of body weight gain was calculated as follows.

$$\frac{\text{Mean final weight} - \text{mean initial weight}}{\text{mean initial weight}} \times 100$$

Statistical analysis

All data was expressed as Mean ± S.D. The data of weekly body weight, body weight gain, hematology were compared by ANOVA. Analyses of data were done using the IBM-SPSS software (version 22) .A 95% confidence level was used to determine statistically significant differences.
If p value <0.05 = Significant
If p value >0.05 = Non significant

RESULT

It is evident that there were no clinical signs or symptoms to indicate that the animals were adversely affected by the doses or treatment given throughout the period of the study. This observation is further supplemented by the fact that all the animals were alive at the end of the study. The results of the body weight of all animals during the study are given in Table 2-4 (Fig.1-6). There was no effect on the mean and percentile body weights of the animals of low dose and intermediate dose groups when compared to their control counterparts, whereas, a significant decrease was observed in the body weight gain of high dose group animals (Table 4 Fig.5). Evaluation of various hematological parameters like Hemoglobin, WBC count, RBC count, hematocrit and platelet count of test and recovery group animals did not reveal any changes when compared with the control group animals (Table 5-8, Fig.7-11). As all the parameters fell within the normal range.

The haematological parameters of all the dose group animals (G2, G3, G4,) were comparable to the parameters of control group animals (G1), when evaluated at 0 day, 45th day and at terminal sacrifice (91 days). Similarly, the parameters of recovery intermediate dose group (G6) animals were comparable to their control counter parts (G5) as the parameters fell within the accepted laboratory limits (Table 5-8, Fig.7-11).

DISCUSSION

The present study results indicate that Fomesafen did not produce any toxic signs and symptoms or mortality therefore indicative of its safety. Based on the observations and results obtained from various studies, it can be said that the Fomesafen technical given to the animals did not show any mortality as well as any adverse impact on the health of animals.

As reported in the literature, the metabolic rate in rats is governed by the functions of liver. The body weight is expected to rise with time at standard laboratory rate. Any deviations on either side i.e. increase or decrease in body weight of the animals would be ascribed to the functioning of the organs mainly the liver. A significant decrease in body weight gain was noticed in the animals of high dose group [Table 3-4, Fig. 3-5]. The exact underlying mechanism of the decreased body weight gain needs to be further clarified.

The Hb concentration and hematocrit generally provide an accurate reflection of the extent to which the circulating red cell mass is reduced.[10] Brar **et al**.[11] suggested that if the PCV is decreased, the animal is anemic whereas an elevated PCV indicate polycythemia. No such finding observed in the results of present study with repeated oral exposure of Fomesafen technical on female wistar rats (Table 5-8, Fig.7-11).

Insecticides like other toxic chemicals are reported to have an adverse effect on bone marrow causing a decrease in erythrocyte production.[12] Decreased erythrocyte production and hypoplasia of erythropoietic tissues have also been demonstrated in severe uremia (increased blood urea nitrogen) associated with renal damage,[13] as is evident in the present study. Exposure of red blood cells (RBCs) to toxicants results in the production and denaturation of metHb production and in the coalescence of Hb molecules to form Heinz bodies. The attachment of Heinz bodies to the plasma membrane increases membrane rigidity and leads to anemia by means of increased RBC lysis or premature removal from circulation[14] No such finding observed in the results of present study with repeated oral exposure of Fomesafen technical on female wistar rats.

TABLE2: MEAN PERCENTILE WEEKLY BODY WEIGHT DATA OF FEMALE RATS

GROUP	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17
Control (0 mg/kg B.wt.)	112.09 ± 1.12	124.07 ± 1.93	134.96 ± 3.25	145.97 ± 3.46	156.63 ± 3.53	167.57 ± 4.11	177.58 ± 5.19	184.94 ± 5.28	192.07 ± 5.99	198.23 ± 6.09	204.56 ± 6.17	210.89 ± 6.39	217.40 ± 6.76	-	-	-	-
Low dose (50 mg/kg B.wt.)	112.30 ± 0.80	124.51 ± 1.25	135.59 ± 1.68	146.49 ± 2.11	157.06 ± 3.07	167.62 ± 4.12	177.23 ± 4.75	184.50 ± 5.04	191.44 ± 5.29	196.99 ± 5.54	203.57 ± 5.59	209.72 ± 5.55	216.48 ± 5.81	-	-	-	-
Intermediate Dose (100 mg/kg B.wt.)	111.78 ± 0.78	123.06 ± 1.56	133.39 ± 1.64	143.57 ± 2.02	154.34 ± 2.51	165.36 ± 2.86	175.15 ± 4.78	182.05 ± 5.01	188.29 ± 6.02	193.74 ± 5.60	199.80 ± 5.79	205.85 ± 5.75	212.08 ± 6.03	-	-	-	-
High dose (250 mg/kg B.wt.)	112.15 ± 0.86	123.85 ± 1.27	134.79 ± 1.69	145.81 ± 2.05	156.78 ± 3.16	168.06 ± 3.93	178.49 ± 4.77	185.24 ± 5.73	189.47 ± 6.37	192.30 ± 6.20	195.65 ± 6.28	198.57 ± 6.26	201.33 ± 6.25	-	-	-	-
Recovery Control (0 mg/kg B.wt)	112.05 ± 3.25	122.06 ± 4.58	133.13 ± 4.52	143.61 ± 4.27	155.03 ± 3.93	165.31 ± 4.39	175.15 ± 4.02	182.65 ± 3.64	189.28 ± 3.47	195.83 ± 2.68	202.11 ± 2.73	206.91 ± 3.32	212.66 ± 3.55	217.46 ± 3.82	222.60 ± 3.99	226.79 ± 4.13	231.06 ± 4.00
Recovery Intermediate Dose (100 mg/kg B.wt.)	111.81 ± 2.99	124.37 ± 3.79	136.14 ± 3.97	146.71 ± 4.12	157.46 ± 4.50	168.54 ± 3.87	178.49 ± 3.99	185.83 ± 4.65	191.32 ± 4.26	196.39 ± 3.97	201.55 ± 4.15	203.38 ± 4.94	211.15 ± 4.13	215.52 ± 4.63	219.80 ± 5.26	223.82 ± 5.95	228.88 ± 6.25

TABLE 3: MEAN WEEKLY BODY WEIGHT DATA OF FEMALE RATS

GROUP	Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17
Control (0 mg/kg B.wt.)	115.40 ± 5.02	129.30 ± 4.47	143.10 ± 4.31	155.60 ± 3.50	168.30 ± 3.97	180.60 ± 4.22	193.20 ± 4.16	204.70 ± 3.62	213.20 ± 4.08	221.40 ± 4.20	228.50 ± 4.01	235.80 ± 4.16	243.10 ± 4.56	250.60 ± 5.08	-	-	-	-
Low dose (50 mg/kg B.wt.)	115.60 ± 3.06	129.80 ± 2.70	143.90 ± 2.60	156.70 ± 2.79	169.30 ± 3.06	181.50 ± 3.50	193.70 ± 4.42	204.80 ± 4.78	213.20 ± 5.12	221.20 ± 4.29	227.60 ± 3.86	235.20 ± 3.39	242.30 ± 3.13	250.10 ± 2.73	-	-	-	-
Intermediate Dose (100 mg/kg B.wt.)	119.00 ± 3.27	133.00 ± 2.94	146.40 ± 2.63	158.70 ± 3.02	170.80 ± 3.12	183.60 ± 2.76	196.70 ± 2.83	208.30 ± 1.77	216.50 ± 1.72	223.90 ± 2.42	230.40 ± 2.12	237.60 ± 2.41	244.80 ± 1.99	252.20 ± 1.93	-	-	-	-
High dose (250 mg/kg B.wt.)	116.30 ± 4.76	130.40 ± 4.72	144.00 ± 4.85	156.70 ± 5.03	169.50 ± 4.97	182.20 ± 3.97	195.30 ± 4.03	207.40 ± 3.98	215.20 ± 3.49	220.10 ± 3.14	223.40 ± 3.57	227.30 ± 3.95	230.70 ± 4.24	233.90 ± 4.31	-	-	-	-
Recovery Control (0 mg/kg B.wt)	114.70 ± 2.21	128.50 ± 3.50	140.00 ± 5.70	152.70 ± 5.76	164.70 ± 5.19	177.80 ± 4.83	189.60 ± 5.87	200.90 ± 5.88	209.50 ± 5.72	217.10 ± 5.43	224.60 ± 4.58	231.80 ± 4.26	237.30 ± 4.72	243.90 ± 4.93	249.40 ± 5.32	255.30 ± 5.48	260.10 ± 5.51	265.00 ± 5.79
Recovery Intermediate Dose (100 mg/kg B.wt.)	114.60 ± 2.63	128.10 ± 3.25	142.50 ± 4.60	156.00 ± 5.12	168.10 ± 5.22	180.40 ± 4.79	193.10 ± 4.25	204.50 ± 4.53	212.90 ± 4.86	219.20 ± 4.73	225.00 ± 3.74	230.90 ± 3.11	236.20 ± 3.26	241.90 ± 2.88	246.90 ± 3.41	251.80 ± 4.16	256.40 ± 5.02	262.20 ± 5.45

TABLE 4: MEAN WEEKLY BODY WEIGHT GAIN DATA OF FEMALE RATS IN MAIN STUDY

GROUP	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17
Control (0 mg/kg B.wt.)	13.90 ± 0.74	27.70 ± 1.16	40.20 ± 2.04	52.90 ± 1.97	65.20 ± 1.48	77.80 ± 1.62	89.30 ± 2.26	97.80 ± 2.25	106.00 ± 2.87	113.10 ± 2.56	120.40 ± 2.41	127.70 ± 2.71	135.20 ± 3.26	-	-	-	-
Low dose (50 mg/kg B.wt.)	14.20 ± 0.63	28.30 ± 0.82	41.10 ± 1.20	53.70 ± 1.64	65.90 ± 2.64	78.10 ± 3.84	89.20 ± 4.39	97.60 ± 4.70	105.60 ± 4.40	112.00 ± 4.32	119.60 ± 4.03	126.70 ± 3.77	134.50 ± 3.69	-	-	-	-
Intermediate Dose (100 mg/kg B.wt.)	14.00 ± 0.67	27.40 ± 1.26	39.70 ± 1.25	51.80 ± 1.55	64.60 ± 1.65	77.70 ± 1.83	89.30 ± 3.43	97.50 ± 3.47	104.90 ± 4.53	111.40 ± 3.86	118.60 ± 3.98	125.80 ± 3.65	133.20 ± 3.74	-	-	-	-
High dose (250 mg/kg B.wt.)	14.10 ± 0.74	27.70 ± 0.95	40.40 ± 1.26	53.20 ± 1.14	65.90 ± 1.20	79.00 ± 1.89	91.10 ± 2.56	98.90 ± 3.25	103.80* ± 3.68	107.10* ± 3.51	111.00* ± 3.68	114.40* ± 3.72	117.60* ± 3.63	-	-	-	-
Recovery Control (0 mg/kg B.wt)	13.80 ± 3.58	25.30 ± 5.14	38.00 ± 5.10	50.00 ± 4.71	63.10 ± 4.28	74.90 ± 5.04	86.20 ± 4.80	94.80 ± 4.49	102.40 ± 4.22	109.90 ± 3.21	117.10 ± 3.00	122.60 ± 3.63	129.20 ± 3.88	134.70 ± 4.27	140.60 ± 4.45	145.40 ± 4.53	150.30 ± 4.64
Recovery Intermediate Dose (100 mg/kg B.wt.)	13.50 ± 3.24	27.90 ± 4.18	41.40 ± 4.43	53.50 ± 4.53	65.80 ± 4.59	78.50 ± 3.75	89.90 ± 3.87	98.30 ± 4.45	104.60 ± 4.06	110.40 ± 3.24	116.30 ± 2.98	121.60 ± 3.37	127.30 ± 2.71	132.30 ± 3.37	137.20 ± 4.21	141.80 ± 5.12	147.60 ± 5.50

Statistical analysis: ANOVA (p value > 0.05)
If p value <0.05 = Significant, If p value >0.05 = Non significant
*=Significant

TABLE 5: MEAN HAEMATOLOGY DATA OF FEMALE RATS [TIME: PRETEST (0 - DAY)]

Parameters	WBC Count ($x 10^3$)	L%	N%	E%	M%	B%	RBC count ($x 10^6$)	Reticulocyte %	Hb Gm %	HCT (PCV) %	Protime (in sec.)	Platelet Count ($x 10^5$)
Control (0mg/kg b.wt)	9.38 ± 0.23	71.70 ± 1.57	22.30 ± 1.64	2.00 ± 0.82	1.70 ± 0.82	0.00 ± 0.00	7.40 ± 0.22	2.60 ± 0.70	13.72 ± 0.44	41.97 ± 1.06	17.70 ± 0.67	7.98 ± 0.29
Low Dose (50mg/kg b.wt))	9.44 ± 0.20	71.51 ± 1.41	22.70 ± 0.95	2.00 ± 0.47	1.90 ± 0.74	0.00 ± 0.00	7.35 ± 0.19	2.10 ± 0.88	13.75 ± 0.43	42.70 ± 0.40	18.10 ± 0.86	8.04 ± 0.36
Intermediate Dose (100mg/kg b.wt)	9.38 ± 0.30	72.40 ± 1.07	22.80 ± 1.40	2.10 ± 0.88	1.80 ± 0.92	0.00 ± 0.00	7.41 ± 0.19	2.50 ± 0.53	13.79 ± 0.58	43.76 ± 1.12	17.90 ± 0.88	8.34 ± 0.18
High Dose (250mg/kg b.wt)	9.47 ± 0.28	72.10 ± 1.37	21.90 ± 2.13	2.20 ± 0.92	2.00 ± 0.82	0.00 ± 0.00	7.44 ± 0.23	2.50 ± 0.71	13.81 ± 0.40	43.60 ± 0.48	17.80 ± 0.63	8.33 ± 0.18
Recovery control (0 mg/kg b.wt)	9.58 ± 0.22	71.80 ± 1.55	23.20 ± 1.87	2.10 ± 0.74	2.00 ± 0.67	0.00 ± 0.00	7.48 ± 0.17	2.60 ± 0.70	13.96 ± 0.39	43.64 ± 0.72	18.10 ± 0.74	8.38 ± 0.18
Recovery intermediate Dose (100mg/kgb.wt)	9.53 ± 0.13	72.70 ± 1.77	22.70 ± 1.16	2.30 ± 0.82	2.30 ± 0.67	0.00 ± 0.00	7.41 ± 0.25	2.60 ± 0.52	13.76 ± 0.47	43.03 ± 1.04	17.90 ± 0.74	8.45 ± 0.21

STATISTICAL ANALYSIS: ANOVA (P VALUE:> 0.05)

TABLE 6: Mean Haematology Data Of Female Rats

Parameters	Control (0 mg/kg B.wt.)		Low Dose (50 mg/kg B.wt.)		Intermediate Dose (100 mg/kg B.wt.)		High Dose (250 mg/kg B.wt.)	
	Day 45th	Day 91st	Day 45th	Day 91st	Day 45th	Day 91st	Day 45th	Day 91st
WBC Count (x 10^3)	11.52 ± 3.16	11.53 ± 2.45	13.07 ± 1.80	9.86 ± 1.63	12.96 ± 2.01	9.35 ± 1.67	10.35 ± 1.67	11.08 ± 1.69
L%	78.80 ± 2.78	78.20 ± 2.94	80.20 ± 2.62	79.90 ± 3.03	75.60 ± 3.41	77.00 ± 2.00	77.30 ± 2.83	76.70 ± 2.54
N%	17.60 ± 1.78	18.40 ± 2.63	16.80 ± 1.87	16.40 ± 2.67	20.90 ± 3.45	19.50 ± 1.78	19.90 ± 3.38	20.00 ± 1.89
E%	1.90 ± 0.57	1.90 ± 0.74	1.50 ± 0.71	2.00 ± 0.82	1.80 ± 0.79	1.90 ± 0.88	1.60 ± 0.70	1.80 ± 0.79
M%	1.70 ± 0.95	1.50 ± 0.71	1.50 ± 0.71	1.70 ± 0.82	1.70 ± 0.67	1.60 ± 0.52	1.20 ± 0.42	1.50 ± 0.71
B%	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
RBC count (x 10^6)	6.37 ± 0.43	6.65 ± 0.67	6.29 ± 0.39	6.80 ± 0.77	6.68 ± 0.38	7.02 ± 0.88	5.89 ± 0.65	6.32 ± 0.37
Reticulocyte %	2.60 ± 0.52	2.00 ± 0.82	2.50 ± 0.53	2.00 ± 0.82	2.40 ± 0.52	2.20 ± 0.79	2.40 ± 0.52	2.00 ± 0.67
Hb Gm %	12.76 ± 0.90	13.24 ± 1.17	12.79 ± 0.89	13.71 ± 1.32	13.25 ± 0.65	13.85 ± 1.06	12.32 ± 1.37	12.67 ± 0.81
HCT %	35.57 ± 2.36	36.95 ± 3.48	35.37 ± 2.47	38.56 ± 3.76	38.05 ± 2.08	39.19 ± 3.48	33.93 ± 4.12	34.72 ± 2.28
Protime (in sec.)	18.10 ± 0.88	17.90 ± 0.74	18.20 ± 1.03	17.80 ± 0.79	18.00 ± 0.82	17.90 ± 0.88	17.90 ± 1.10	17.80 ± 1.14
Platelet Count(x10^5)	8.09 ± 0.97	8.51 ± 0.45	8.20 ± 0.77	9.08 ± 0.60	8.89 ± 0.52	8.54 ± 1.04	8.59 ± 0.75	8.47 ± 0.83

STATISTICAL ANALYSIS: ANOVA (P VALUE:> 0.05)

TABLE 7: Mean Haematology Data Of Female Rats [Time: Interim Study/During Dosing Period On (45th Day) (Recovery Group)]

Parameters	WBC Count (x 10^3)	L%	N%	E%	M%	B%	RBC count (x 10^6)	Reticulocyte %	Hb Gm %	HCT %	Protime (in sec.)	Platelet Count (x 10^5)
Recovery Control (0 mg/kg b.wt)	12.45 ± 2.27	78.70 ± 3.74	18.80 ± 3.94	1.30 ± 0.48	1.20 ± 0.42	0.00 ± 0.00	6.21 ± 0.46	2.30 ± 0.48	12.64 ± 0.89	35.09 ± 3.08	15.00 ± 6.67	8.42 ± 0.90
Recovery Intermediate Dose (100 mg/kgb.wt)	12.72 ± 1.84	79.40 ± 2.76	17.60 ± 1.90	1.70 ± 0.82	1.30 ± 0.67	0.00 ± 0.00	6.33 ± 0.41	2.60 ± 0.52	12.53 ± 0.85	35.35 ± 2.75	15.50 ± 7.18	8.08 ± 0.92

Statistical analysis: ANOVA (p value:> 0.05)

TABLE 8: Mean Haematology Data Of Female Rats [Time: Terminal Sacrifice (119th Day) (Recovery Group)]

Parameters	WBC Count (x 10^3)	L%	N%	E%	M%	B%	RBC count (x 10^6)	Reticulocyte %	Hb Gm %	HCT %	Protime (in sec.)	Platelet Count (x 10^5)
Recovery Control (0 mg/kg b.wt)	10.64 ± 2.26	77.10 ± 2.56	19.20 ± 1.99	2.30 ± 0.67	1.40 ± 0.52	0.00 ± 0.00	6.82 ± 0.89	2.00 ± 0.67	13.53 ± 1.18	37.93 ± 3.38	18.20 ± 1.14	8.39 ± 0.72
Recovery Intermediate Dose (100 mg/kgb.wt)	10.88 ± 2.43	77.80 ± 2.82	18.30 ± 2.63	2.30 ± 0.67	1.60 ± 0.70	0.00 ± 0.00	6.86 ± 1.09	2.00 ± 0.67	12.98 ± 1.08	36.33 ± 3.09	18.20 ± 1.03	7.99 ± 1.11

STATISTICAL ANALYSIS: ANOVA (P VALUE:> 0.05)

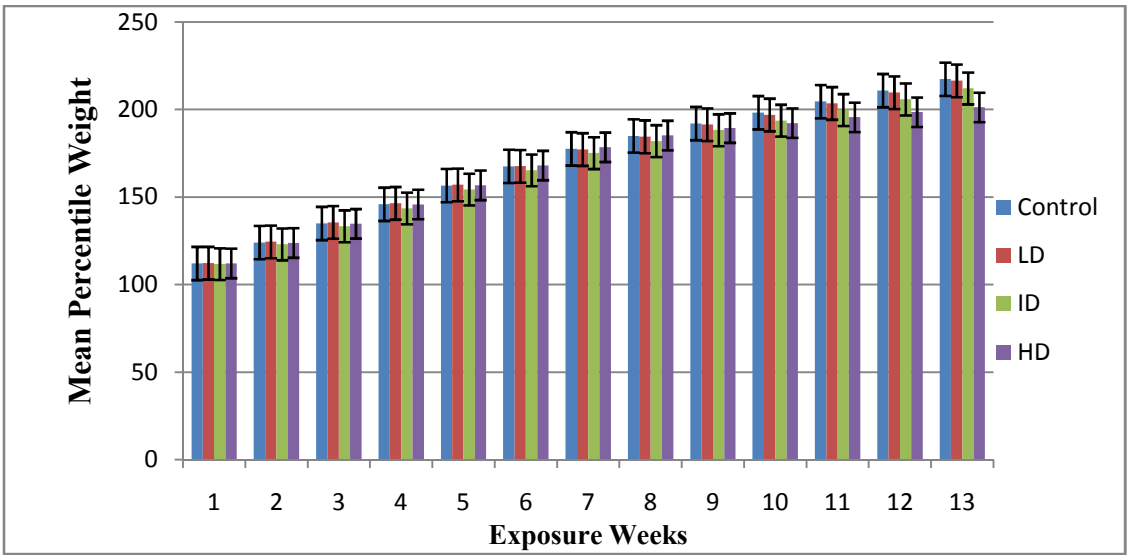

Fig.1 Mean Percentile Body Weight - Main Study Groups

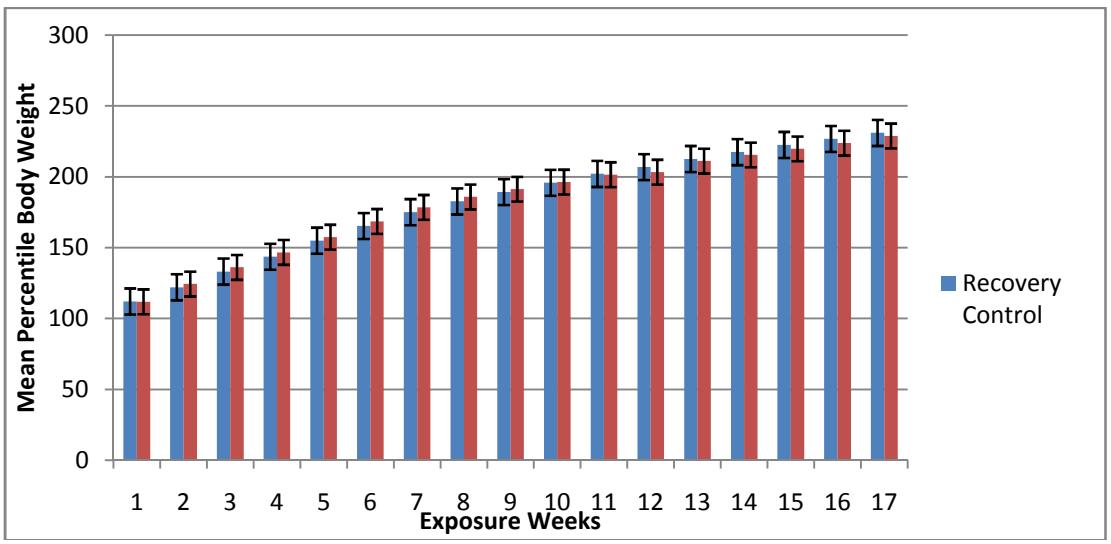

Fig.2 Mean Percentile Body Weight - Recovery Study Groups

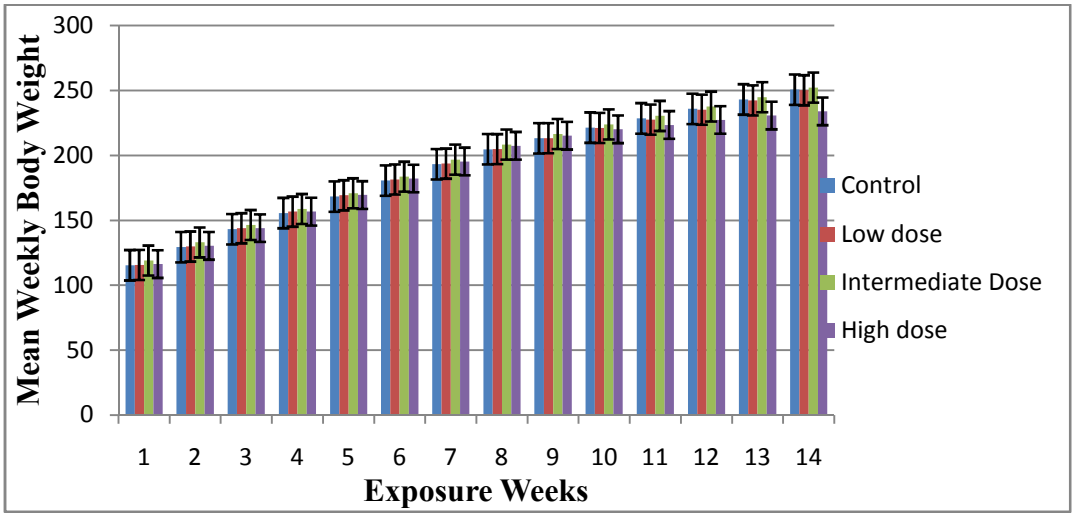

Fig. 3 Mean Weekly Body Weight - Main Study Groups

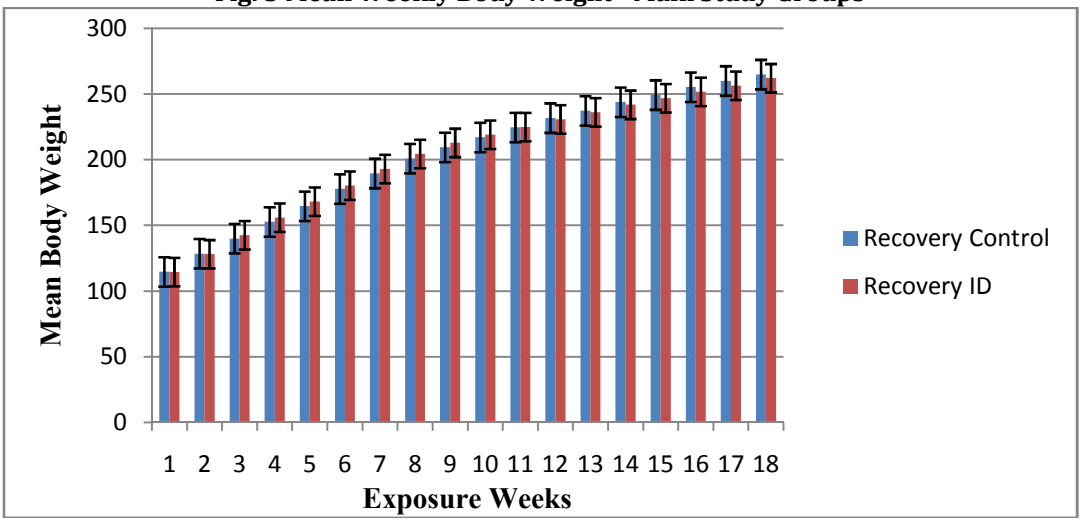

Fig. 4 Mean Weekly Body Weight - Recovery Study Groups

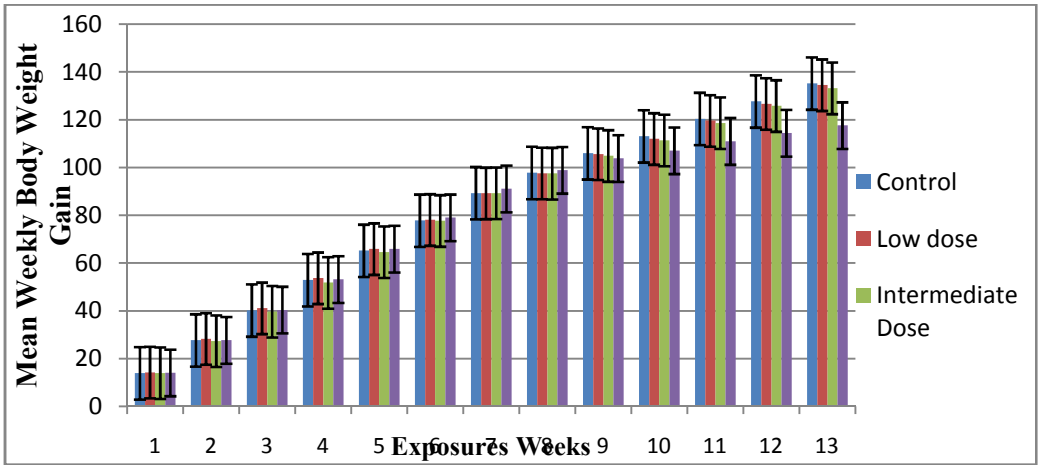

Fig. 5 Mean Weekly Body Weight Gain - Main Study Groups

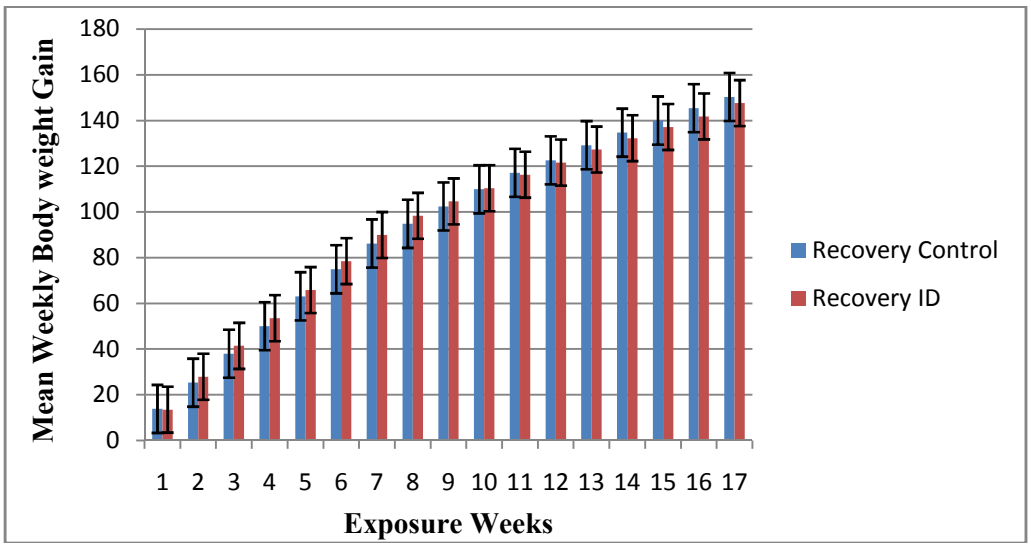

Fig. 6 Mean Weekly Body Weight Gain - Recovery Study Groups

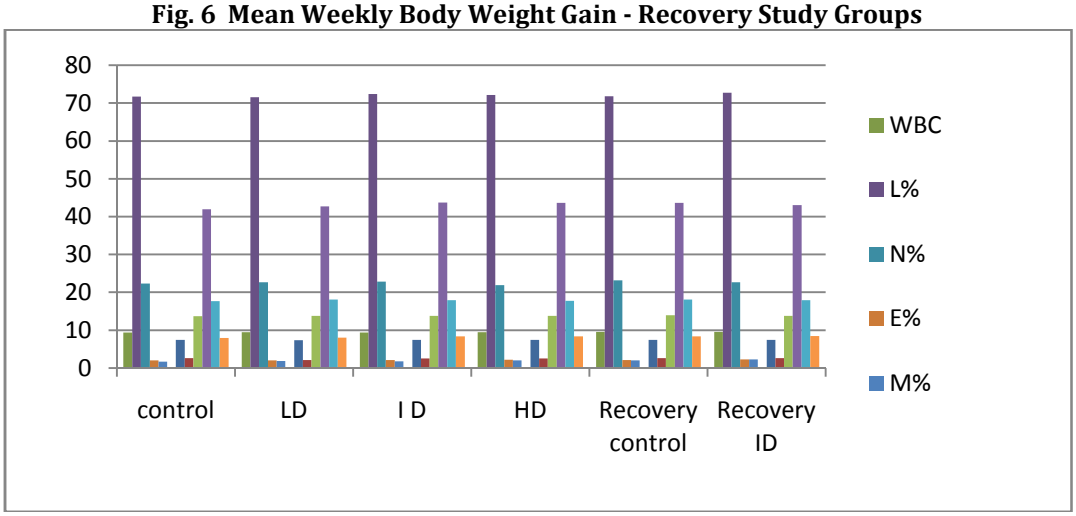

Fig.7 Hematology Data -Day 0 (Pre-test)

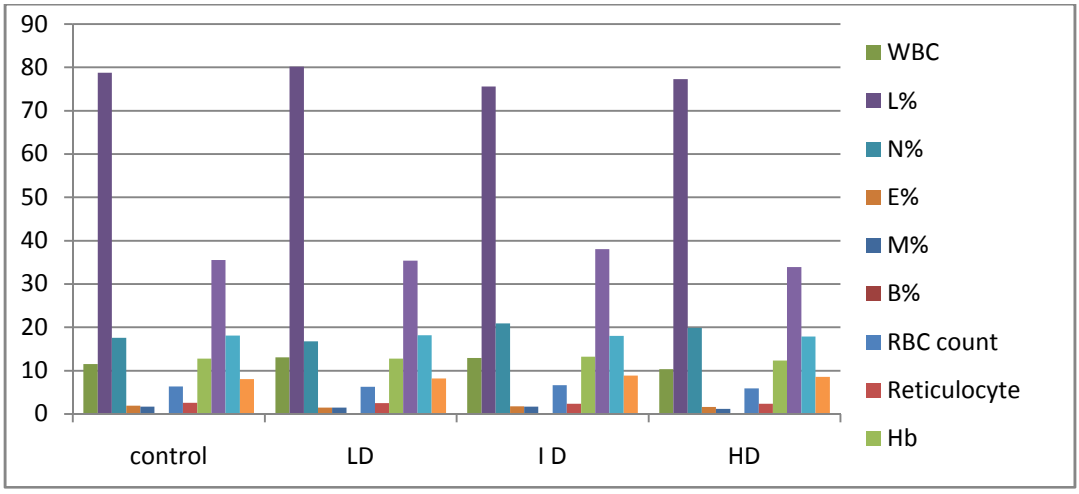

Fig.8 Mean Heamatology Data -45 days

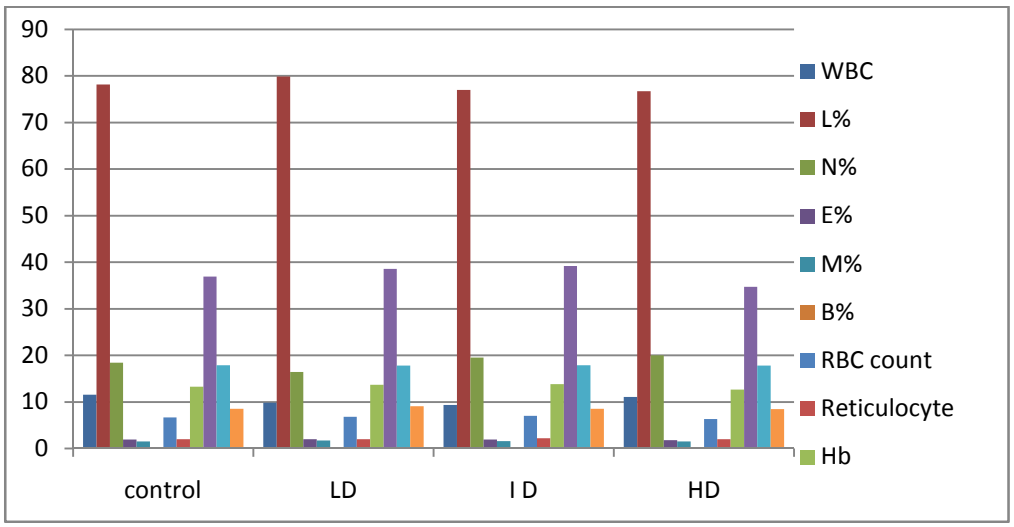

Fig.9 Mean Heamatology Data -91 days

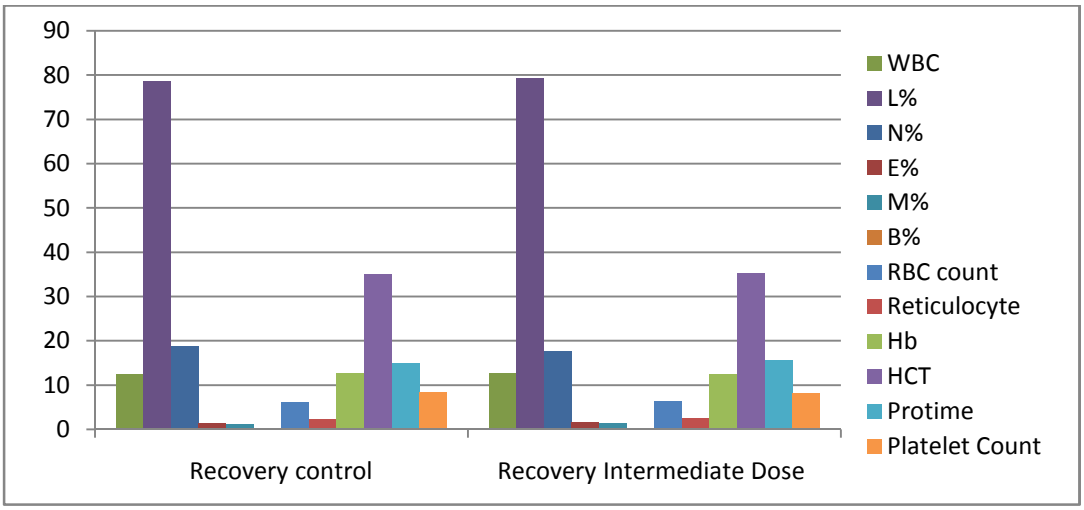

Fig.10 Mean Hematology Data - Recovery Group (45 days)

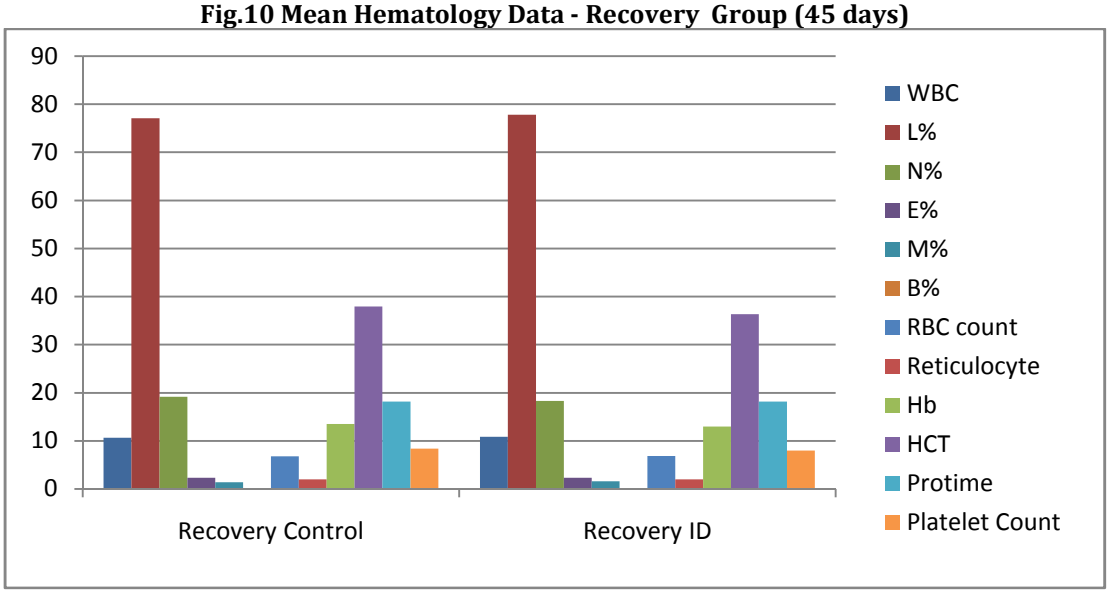

Fig.11 Mean Hematology Data - Recovery Group (119 days)

CONFLICT TO INTEREST: None

REFERENCES

1. Rao, AN and Nagamani A (2013). Eco-efficient weed management approaches for rice in tropical Asia. Proc. 4th Tropical Weed Science Conf. Weed Management and Utilization in the Tropics held during January 23-25,2013, The Empress Hotel, Chiang Mai, Thailand, p. 78-87.
2. Rao, AN and Nagamani A (2010) Integrated Weed Management in India-Revisited. Indian J. Weed. Sci. 42: 1-10.
3. Bhan VM, Sushilkumar and Raghuwanshi MS (1999) Weed Management in India. Indian J. Plant Prot. 17: 71- 202.
4. DWSR/2013. Vision 2050.' Directorate of Weed Science Research, Jabalpur, India.
5. Yaduraju NT (2012) Weed management perspectives for India in the changing agriculture scenario in'the'-country. Pak. J. Weed Sci. Res. 18 (Spl. Issue): 703-710.
6. Philips McDougall (2013) [Online]. Available: http://phillipsmcdougall.co.
7. Zhang ZP (2003) Development of chemical weed control and integrated weed management in China. Weed Biol. Manag. 3:197–203
8. Masthan SC, Reddy KA, Reddy TR and Rao LJ (1989). Increasing the productivity of rice, maize and groundnut in farmers' fields in Andhra Pradesh through weed control. Pesticides, 23(6):42–44.
9. Manda P (2011) Evaluation report on the impact of spray service technology uptake on small-scale farmer livelihoods in Zambia. CARE, Zambia.
10. Brar RS, Sandhu HS, Singh A. (2002). Veterinary Clinical Diagnosis by Laboratory Methods. 1st ed. New Delhi: Kalyani Publishers; 2002.
11. Cowell RL (2004). Veterinary Clinical Pathology Secrets. St. Louis, Missouri: Elsevier Mosby
12. Jain NC (1986). Schalm's Veterinary Haematology. 4th ed. Philadelphia, PA: Lea and Febiger; 1986.
13. Gossett KA (2004). Schalm's Veterinary Haematology. 5th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. Anemias associated with drugs and chemicals; pp. 185–8.
14. Chauhan A, Goyal P, Verma A and Jindal T (2015) Microbiological evaluation of drinking water sold by roadside vendors of Delhi, India. Appl Water Sci, DOI 10.1007/s13201-015-0315-x.
15. Chauhan A and Goyal P (2013). Isolation and Identification of Escherichia coli from various foodstuffs and their resistance against clinically significant antibiotics, J. Advance in Biology, 2, 45-53.
16. Chauhan A, Goyal P, Aggarwal ML and Chacko KM (2013). Prevalence and antibiotic resistance of Bacillus strains isolated from various food stuffs. Journal of Biomedical and Pharmaceutical Research, 2(3), 08-16.
17. Paliwal A, Chauhan A, Agarwal ML, Chacko KM and Jindal T (2017). Physiological and Biochemical Evaluation of Fomesafen Toxicity in Female Albino Wistar Rats, International Journal of Current Microbiology and Applied Sciences, Vol. 6(3) issue (March-2017)