

Mitigating the Effect of *Terminalia chebula* Retz., *Terminalia bellirica* (Gaertn) Roxb. and *Phyllanthus emblica* L. on Imidacloprid Insecticide Induced Toxemia in Albino Wistar Rats

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Abstract: Indiscriminate usage of pesticides in agriculture is leading to contamination of environment and natural resources thereby producing an adverse impact on animal and human health. Administration of Imidacloprid through various routes in animals produces marked alterations in serum biochemical and haematological parameters. Healthy adult female rats (*Rattus norvegicus*) were administered IMI at the dose of 40mg/kg body weight, 80mg/kg body weight orally. Both doses were given individually to investigate the IMI toxicity and its reversal by *Terminalia chebula*, *Terminalia bellirica*, *Phyllanthus emblica* and *Triphala* (1:1:1). The results revealed that 28 days of exposure insignificant haematological changes in comparison to the control group. This study exhibited that sub-acute oral administration of Imidacloprid at this particular dose of 40mg/kg, 80mg/kg body weight causes mild toxic effect on various haematological parameters in rats.

Keywords: Mitigating, Toxemia, Imidacloprid

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I. Introduction

Blood is most important and abundant body fluid. Its composition often reflects the total physiological condition [1]. The blood cells are the mobile units of the body's protective system [2]. Blood being the medium of intercellular and intracellular transport, which comes direct contact with various organs and tissues of the body. The physiological state of an animal and at a particular time is reflected in its blood. Thus blood provides an ideal medium for toxicity studies. The blood parameters have been considered as diagnostic indices of pathological condition, findings are important for the assessment of systemic functions and overall health of animals. Furthermore, the findings also help in diagnosing the structural and functional status of animals exposed to the toxicant [3]; [4].

It is important in toxicological research because a haematological alteration is a good method for rapid evaluation of the chronic toxicities of a compound. A thin epithelial membrane separates fish blood from the water, any unfavourable changes in water body is reflected in blood [5]. Blood composition is altered during disease or malnutrition condition [6].

Toxicological effects on hematological and biochemical parameters in adult rats following oral administration by different doses of each pesticide for 30 days, which is equal to those residues found in and on cucumber fruits after zero time, although there is a large body of literature addressing immune responses during insecticide exposure, the immunotoxicity of IC is poorly understood. Due to its importance in assessing drugs and non-drug chemicals, immunotoxicity testing is required by many regulatory agencies [7].

Subacute toxicity of Imidacloprid was studied in adult male rats following intraperitoneal administration @ 20 and 40 mg/kg daily for 28 days. There was no effect on Hb level, PCV, TLC, lymphocyte, neutrophil, eosinophil counts and total erythrocyte counts at both the dose levels [8]. Using pesticide is an important procedure for enhancing agriculture yield. However, the great consciousness, brought back upon their deleterious effects on human, animal and environmental health, lead to the shortage of their use by imposing various rules [9]. Identification of phytochemicals present in triphala methanol fruit extracts and evaluated their major compounds present and its nature and activities with the aid of GC-MS technique which may provide an insight to the researchers [10]. *Terminalia chebula* has phytoconstituents such as tannin, flavonoids, alkaloids, carbohydrates, glycosides, saponin, protein, aminoacids, polyphenol, quinine and coumarin [11]. Mother Nature

has gifted mankind with tremendous medicinal plants to create a disease free and healthy life. The present work is a trial to understand the haematological alterations of Imidacloprid and important medicinal recovery of *Terminalia chebula*, *Terminalia bellirica*, *Phyllanthus emblica* and triphala emphasizing the mechanisms behind the activities and enlighten the therapeutic applications and clinical trials.

II. Materials And Methods

2.1 Sample Collection and authentication

Fresh fruits of *Terminalia chebula* Retz., *Terminalia bellirica* Roxb. and *Phyllanthus emblica* L. were collected from hill areas, Athipattu (Thiruvannamalai), Therambattu (Vellore) and Sirumalai (Dindugal). Samples were identified and authenticated by Dr. John Britto, Rapinet Herbarium, St. Joseph's College, Trichy, Tamilnadu, India and given the Voucher Specimen No.VEA/001/2013, VEA/002/2013 and VEA/003/2013 respectively.

2.2 Preparation of Extract

Fruits of *Terminalia chebula*, *Terminalia bellirica* and *Phyllanthus emblica* were shade dried, pericarp and mesocarp of fruits were pulverized into fine powder individually and formulated in 1:1:1 ratio. Extracts were prepared by using Soxhlet extractor and 95% Methanol were used as solvent, the residue was filtered and concentrated under reduced pressure by rotary evaporator. The final extracts were stored in closed containers until further analysis [12].

2.3 Experimental Animals

Female albino wistar rats were selected as experimental model between 6-8 weeks weighing and 160-180grams were procured from Central Animal Facility, SASTRA University, Thanjavur, Tamilnadu, India. The experiments were carried out as per the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi, India and approved by the Institutional Animal Ethical Committee (IAEC), SASTRA University (Approval Number: 302/SASTRA/IAEC/RPP dated 29.04.2014).

2.4 Haematological parameters

The parameters included: Red Blood Cell (RBC) count [13], Haemoglobin (Hb) [14], Hematocrit (Ht) [15], Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW), Reticulocyte Count [16]. Total Leucocyte Count (TLC), Neutrophils (NE), Eosinophil (EO), Basophils, Lymphocytes (LY), Monocytes (MO) [17] and Platelets (PLT) [18] were estimated with the help of hematology analyzer.

III. Results

Table -1 Change in the level of haematological parameters (Red Blood Cells)

Treatment	HCT (%)	RBC (10 ¹² /L)	HB (g/dl)	MCV (fl)	MCH (pg)	MCHC (g/dl)	RDW (%)	Retic (10 ⁹ /L)	Retic (%)
Control	47.80±1.10 ^a	7.79±0.43 ^a	12.93±0.19 ^a	61.43±3.27 ^a	16.65±0.55 ^a	27.25±0.48 ^a	13.67±1.93 ^a	219.02±35.58 ^a	2.16±0.99 ^a
IMI (40mg/kg)	47.77±1.61 ^a	5.78±0.68 ^b	8.20±0.41 ^b	72.80±1.92 ^b	25.97±2.21 ^b	36.07±1.49 ^b	12.95±0.88 ^a	13.25±0.22 ^b	1.71±0.22 ^b
IMI (80mg/kg)	44.67±1.47 ^a	5.51±0.46 ^c	7.20±0.30 ^c	77.87±2.45 ^c	44.05±2.21 ^c	41.72±3.16 ^c	13.10±1.07 ^a	144.18±2.85 ^c	2.13±0.02 ^a
IMI 40mg + <i>T. chebula</i>	50.63±2.05 ^b	8.20±0.44 ^a	13.38±0.69 ^a	61.45±1.16 ^a	16.15±0.79 ^a	26.27±0.81 ^a	13.28±1.14 ^a	70.05±19.35 ^d	0.98±0.27 ^b
IMI 80mg + <i>T. chebula</i>	45.38±2.52 ^a	7.55±0.64 ^a	12.32±0.58 ^a	58.52±3.86 ^a	16.06±0.85 ^a	26.57±0.23 ^a	13.33±0.68 ^a	32.87±3.61 ^b	0.46±0.08 ^c
IMI 40mg + <i>T. bellirica</i>	47.47±2.09 ^a	7.94±0.32 ^a	12.53±0.60 ^a	60.27±0.72 ^a	16.08±0.51 ^a	26.38±0.48 ^a	14.53±2.02 ^a	168.07±18.45 ^c	1.63±1.07 ^a
IMI 80mg + <i>T. bellirica</i>	48.13±1.34 ^b	8.22±0.40 ^b	13.22±0.53 ^a	61.00±3.50 ^a	16.35±0.27 ^a	26.77±1.09 ^a	14.33±1.47 ^a	142.98±73.77 ^c	1.80±1.02 ^a
IMI 40mg + <i>P. emblica</i>	45.27±3.19 ^a	7.33±0.22 ^a	12.21±0.89 ^a	62.25±3.67 ^a	15.43±1.71 ^a	26.72±0.39 ^a	14.12±1.26 ^a	161.52±10.94 ^c	1.97±1.10 ^a
IMI 80mg + <i>P. emblica</i>	47.00±1.11 ^a	7.93±0.29 ^a	12.70±0.33 ^a	59.62±1.08 ^a	16.23±0.24 ^a	27.45±0.41 ^a	13.68±0.89 ^a	65.15±2.74 ^b	0.63±0.29 ^c
IMI 40mg + Triphala	49.15±4.81 ^c	7.91±0.97 ^a	12.33±0.99 ^a	58.80±1.08 ^a	16.07±0.89 ^a	26.98±1.57 ^a	17.67±4.87 ^b	33.76±10.70 ^b	0.77±0.71 ^c
IMI 80mg + Triphala	51.15±3.61 ^d	7.97±0.45 ^a	12.87±0.29 ^a	61.35±2.04 ^a	16.15±0.48 ^a	26.10±1.66 ^a	20.22±2.49 ^b	44.02±3.00 ^b	0.64±0.06 ^c

Table -2 Changes in the level of haematological parameters (White Blood Cells)

Treatment	WBC 10 ⁹ /L	NE 10 ⁹ /L	LY 10 ⁹ /L	MO 10 ⁹ /L	EO 10 ⁹ /L	NE %	LY %	MO %	EO %
Control	7.11±1.2 6 ^a	3.37±1.5 1 ^a	5.34±1.1 1 ^a	0.77±0.2 8 ^a	0.01±0.0 1 ^a	18.74±3. 10 ^a	69.53±5. 34 ^a	10.27±5. 59 ^a	0.06±0.0 2 ^a
IMI (40mg/kg)	14.42±3. 72 ^b	8.71±2.1 6 ^b	5.75±1.3 3 ^b	1.90±0.9 5 ^b	1.01±0.0 4 ^b	34.99±18 .59 ^b	52.86±21 .64 ^b	8.80±3.7 7 ^a	0.05±0.0 2 ^a
IMI (80mg/kg)	17.11±1. 26 ^b	12.28±3. 67 ^c	13.89±2. 34 ^c	35.10±1. 63 ^c	3.52±2.5 2 ^c	36.58±10 .63 ^c	51.96±11 .08 ^b	10.65±1. 29 ^a	0.72±0.2 5 ^b
IMI 40mg + <i>T. chebula</i>	10.33±3. 16 ^a	4.07±1.6 9 ^b	8.14±2.7 6 ^a	0.99±0.7 4 ^a	0.29±0.1 3 ^a	21.96±5. 68 ^a	72.46±7. 24 ^a	6.79±2.6 6 ^a	0.11±0.0 7 ^a
IMI 80mg + <i>T. chebula</i>	7.71±1.1 6 ^a	2.56±0.5 3 ^a	4.96±2.1 3 ^a	0.53±0.1 2 ^a	0.02±0.0 1 ^a	23.80±2. 77 ^a	68.33±4. 41 ^a	7.47±1.3 0 ^a	0.12±0.0 8 ^a
IMI 40mg + <i>T. bellirica</i>	9.05±3.2 0 ^a	3.07±1.3 0 ^a	5.92±2.6 0 ^a	0.34±0.0 7 ^a	0.02±0.0 1 ^a	27.22±7. 35 ^a	67.02±6. 81 ^a	5.99±2.0 6 ^a	0.14±0.1 5 ^a
IMI 80mg + <i>T. bellirica</i>	7.94±1.6 9 ^a	4.47±2.5 1 ^a	6.77±1.9 6 ^a	0.51±0.1 2 ^a	0.01±0.0 1 ^a	29.73±3. 79 ^b	64.83±3. 50 ^a	5.97±0.9 0 ^a	0.23±0.0 7 ^a
IMI 40mg + <i>P. emblica</i>	9.74±2.1 7 ^a	3.54±2.0 0 ^a	7.52±2.4 8 ^a	0.39±0.1 2 ^a	0.01±0.0 0 ^a	25.53±2. 18 ^a	69.78±5. 36 ^a	5.57±1.9 3 ^a	0.18±0.0 8 ^a
IMI 80mg + <i>P. emblica</i>	7.58±1.3 7 ^a	3.36±1.9 7 ^a	7.33±2.2 4 ^a	0.39±0.1 2 ^a	0.01±0.0 0 ^a	27.30±6. 03 ^a	67.94±7. 19 ^a	6.07±2.3 3 ^a	0.12±0.0 5 ^a
IMI 40mg + Triphala	8.59±3.9 9 ^a	3.65±0.9 3 ^a	6.72±2.9 7 ^a	0.40±0.1 7 ^a	0.03±0.0 2 ^a	20.99±4. 73 ^a	69.60±6. 03 ^a	6.72±2.9 9 ^a	0.43±0.3 3 ^{ab}
IMI 80mg + Triphala	8.10±1.1 1 ^a	3.28±1.7 0 ^a	5.90±1.2 3 ^a	0.48±0.1 4 ^a	0.05±0.0 4 ^a	26.21±4. 38 ^a	67.96±3. 74 ^a	6.66±1.9 6 ^a	1.01±0.8 8 ^c

Table -3 Changes in the level of haematological parameters (Platelets)

Treatment	Platelets (PCT %)	Platelets (MPV fl)	Platelets (PDW %)	Platelets (PLT 10 ⁹ /L)
Control	0.47±0.06 ^a	8.72±0.29 ^a	28.95±0.89 ^a	531.17±59.31 ^a
IMI (40mg/kg)	0.30±0.10 ^a	6.48±0.54 ^b	30.18±1.59 ^a	913.00±860.06 ^b
IMI (80mg/kg)	0.27±0.03 ^b	7.98±0.33 ^c	29.37±0.60 ^a	429.67±135.37 ^a
IMI 40mg + <i>T. chebula</i>	0.34±0.02 ^a	8.08±0.23 ^c	31.72±8.08 ^a	444.50±57.45 ^a
IMI 80mg + <i>T. chebula</i>	0.38±0.06 ^a	8.07±0.08 ^c	28.58±0.16 ^a	442.50±20.25 ^a
IMI 40mg + <i>T. bellirica</i>	0.40±0.06 ^a	8.03±0.18 ^c	29.80±2.10 ^a	533.83±106.11 ^a
IMI 80mg + <i>T. bellirica</i>	0.35±0.07 ^a	8.18±0.17 ^c	28.62±0.22 ^a	487.50±28.28 ^a
IMI 40mg + <i>P. emblica</i>	0.37±0.06 ^a	8.07±0.15 ^c	28.93±0.51 ^a	408.17±80.57 ^a
IMI 80mg + <i>P. emblica</i>	0.48±0.25 ^a	8.05±0.19 ^c	28.32±0.34 ^a	483.33±18.62 ^a
IMI 40mg + Triphala	0.41±0.01 ^a	7.95±0.20 ^c	28.52±1.01 ^a	610.50±292.52 ^a
IMI 80mg + Triphala	0.42±0.01 ^b	7.30±0.51 ^d	30.07±1.08 ^a	679.00±393.43 ^a

Values are expressed as Mean ± SD for five rats Mean values within the column followed by different letters (Superscript) are significantly ($P < 0.05$) different from each other and same letter are non-significant were comparison by Duncan's multiple range test (DMRT).

IV. Discussion

Imidacloprid exposure leads to marked alterations in serum biochemical and haematological parameters. Imidacloprid was found to be a potent toxic agent, to prevent adverse effects of imidacloprid, it should be used in limited dose for crop protection. Imidacloprid did not produce any significant changes in both hematological and biochemical activity indicates after 28 days of administration. In contrary to this study, it was found that imidacloprid decrease the level of creatinine on 28th day [19]. Insignificant changes in hematological parameters (Hb, PCV, TEC, TLC and DLC) were observed in natural cases of imidacloprid toxicity in buffaloes [20].

Oral administration of imidacloprid at the rate of 80 mg/kg b. wt for 28 days in male albino rats produced a significant decrease in TEC, Hb, PCV, MCV, MCH and MCHC and a significant increase in TLC, whereas co-administration of vitamin-C brought mild to moderate improvement in all these parameters [21]. Imidacloprid did not cause any significant changes in lymphocyte, neutrophil and eosinophil counts in treated rats [22].

RBC, Hb content and Ht values resulting in hypochronic anaemia which was attributed to deficiency of iron and decreased utilization for Hb synthesis. Oxygen carrying capacity of blood also declined in metal exposed *P. parrah* due to the reduction of RBC count and Hb content [23]. Swelling of the red blood cells (erythrocytes) may be due to an increase in protein and carbon dioxide in the blood [24]. Haematological indices

(RBC count, concentration of haemoglobin and haematocrit) have been reported to indicate secondary responses of an organism to irritants [25].

Oral administration of imidacloprid at 0.21 mg/kg b.wt for 28 days in male albino rats produced a significant increase in total leucocyte count [26]. There was a gradual decrease in erythrocyte count, haemoglobin content and the number of platelets in mice treated with metalaxyl fungicide [27]. Reduction in platelet count and disturbed blood clotting was also reported in a subchronic imidacloprid toxicity study in female wistar rats [28].

The depression in RBC's count and rise in Hb contents and red cell indices including MCV, MCHC, MCH recorded in the present work in case of acute group is a clear suggestive to a megaloblastic picture of RBCs and could be attributed to disturbed hematopoiesis, destruction of erythrocytes and reduction in the rate of their formation and/or their enhanced removal from circulation. Erythrocyte damage is presumed to be related to direct oxidative injury to the red cells by the chemicals or to the pitting function of the spleen. It may be assumed that the free radicals resulting from TAA metabolism caused liver injury [29].

An increase, in number of leucocyte precursor cells in the bone marrow or their increased release from bone marrow storage pools, decreased margination of leucocytes into vessel walls and their decreased extravasations from the vessels into tissues [30]. Neutrophils and their derived cytokines play a crucial role in the development and manifestation of inflammation. The stimulation of neutrophils can lead to the production of oxygen derived free radicals also called reactive oxygen species (ROS) that cause further cellular damage [31].

Decreased percentage of lymphocytes and total leucocyte count in Imidacloprid treated high dose indicated a risk to lymphopaenia and immune modulation [32]. Imidacloprid insecticide induced significant increases in the total leucocyte counts of male albino rats. This increase may be related to an increase in lymphocyte number. Phagocytosis is the principal mechanism used by mammals to destroy extracellular pathogens and several viral and fungal organisms [33]. The significant decrease in the RBC, Hb and Haematocrit may be a consequence of severe haemorrhage which results in the dilution of blood caused due to the influx of cells and fluids from body stores [34]; [35]. Blood acts as an internal transport and plays a significant role in the regulation of life activities. It may be described as a specialized fluid connective tissue in which the components are suspended. Neutrophil, Lymphocyte, Monocyte and Eosinophil counts shown slight variation, while administered with Imidacloprid, which was compared with control group. However the mean values of total leucocyte count and monocyte were increased in 80mg/kg/b.w treated animals, which might be due to the rebound effect of Imidacloprid on haemopoietic tissues. There were no significant changes observed in platelet count treated with insecticide Imidacloprid. Administered with *Terminalia chebula*, *Terminalia bellirica*, *Phyllanthus emblica* and Triphala all groups reached the normal levels due to the phytoconstituents present.

V. Conclusion

Current study was under taken to scrutinize mitigate role of *Terminalia chebula*, *Terminalia bellirica*, *Phyllanthus emblica* and Triphala on IMI induced blood toxicity. It deals with the evaluation of the effect of sub-acute toxicity of 28-days oral exposure to Imidacloprid and its subsequent analysis of haematological parameters. Variations were remarkably ameliorated in all the parameters following co-supplementation of selected drugs. Medicinal plant deserves a special attention of the scientific fraternity to emerge as a milestone for medical science of this millennium due to its medicinal properties.

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