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Pathomorphological Studies of Acephate induced toxicity in male wistar rats and its amelioration by *Swertia chirata*

Bhagyashree G Shingumare[1*], Santosh D Moregaonkar[2], Govind R Gangane[3], Saurabh S Rajurkar[4]

[1] Student, Department of Veterinary Pathology, College of Veterinary and Animal Sciences, Parbhani, Maharashtra Animal & Fishery Sciences University, Nagpur, Maharashtra, India

[2] Professor & Head, Department of Veterinary Pathology, College of Veterinary and Animal Sciences, Parbhani, Maharashtra Animal & Fishery Sciences University, Nagpur, Maharashtra, India

[3] Associate Professor, Department of Veterinary Pathology, College of Veterinary and Animal Sciences, Parbhani, Maharashtra Animal & Fishery Sciences University, Nagpur, Maharashtra, India

[4] Student, Department of Veterinary Pharmacology & Toxicology, College of Veterinary and Animal Sciences, Parbhani, Maharashtra Animal & Fishery Sciences University, Nagpur, Maharashtra, India

Abstract
An experimental trial was conducted on thirty male wistar rats to study acephate induced pathomorphological alterations in male Wistar rats and its amelioration by *S. chirata*. The study was conducted for twenty eight days and evaluated by recording clinical signs, body weight, relative organ weights and observing gross and histopathological alterations in visceral organs at the end of trial.

Group II and group IV male rats showed prominent clinical signs such as increased salivation, piloerection, lethargy, increased urine output, diarrhoea and hair loss (from 14th day onward), Body weight (from 14th day onward) and Relative organ weights at 28th day interval were significantly decreased in a rats of group II and IV. No appreciable gross changes were recorded in organs, except, there was focal areas of necrosis and mild to moderate congestion in liver of rats of group II and IV. Histologically, alterations recorded were haemorrhages, degenerative and necrotic changes in Liver and Kidney sections; marked depopulation of lymphocytes in spleen; catarrhal enteritis with MNC infiltration in Intestines; depopulation of spermatogonial cells with emptying of seminiferous tubules in Testes; degenerative and necrotic changes in neurons with vacuolations in parenchyma of Brain. These appreciable changes showed improvement due to *S. chirata.*

Keywords: acephate, pathomorphological alterations, male wistar rats, *S. chirata*

1. Introduction
India is one of the countries of intensive agricultural production and there is high use of pesticide for more crop production. Man is the ultimate consumer of pesticide residues. Through fodder, water, air and other feed stuff pesticide residues reaches in animal and then through milk, meat, egg and other animal products accumulates in human beings. The widespread and misuse of the toxic pesticides created an awareness of potential health hazards and the need to protect the consumer from residues in food. About 20% of Indian food products contain pesticide residues above tolerance levels as compared to only 2% globally [15].

Pesticides are the most common xenobiotics present in the environment and causing toxicity. Prolong exposure of pesticides affected the normal functioning of different organ system and produced many clinical effects [2, 19]. Pesticides, such as acephate, have become a public health concern because pesticide exposure leads to harmful effects in human metabolism, such as hyperglycemia, lipid metabolism dysfunction, DNA damage, increased oxidative stress and cancer, which are rapidly growing epidemics and which lead to increased morbidity and mortality rates and soaring health-care costs [5].

Acephate can over stimulate the nervous system causing nausea, dizziness, confusion and at very high exposures (accidents or major spills), respiratory paralysis and death. Acephate administration causes cytotoxicity and genotoxicity [7] and affects spermatogenesis [12]. A number of studies showed the toxicity of acephate on different organisms, which indicated it as a potent neurotoxic, mutagenic, carcinogenic and cytotoxic compound [20].

In India, hepatoprotective medicinal plants and their formulations have been traditionally used in Ayurveda for the prevention and treatment of diverse liver diseases. In Ayurveda, *Swertia chirata* is used as antipyretic, anthelmintic, anti-inflammatory, anti-carcinogenic, anticholinergic, antioxidant, antimalarial, hypoglycemic, in mutagenicity laxative, in asthma and in leucorrhoea. In Unani system the plant is used as astringent, tonics, stomachic, lessens inflammation, sedative to pregnant uterus and chronic fever [13]. The herbal drug "chirata" obtained from the dried plants of Swertia species. The whole plants of *Swertia* are medicinal but roots are the most powerful parts [1]. In Indian medicinal system, chirata is used as remedy for bronchial asthma, liver disorders, chronic fever, anemia, stomachic and diarrhoea. Considering scenario of use of pesticide, also, treatment of using herbal therapies, the study was conducted with following objective.

2. Objective
1. To asses subacute Acephate toxicity and its amelioration by *S. chirata* through pathomorphological studies.

3. Materials and Methods

3.1 Experimental animals

A total of 30 male Wistar rats ageing about 4-6 weeks and approximately 140-150gms of weights were divided into five groups, each comprising of 6 rats and were maintained for 28 days. The experimental male Wistar rats were procured from M/S Wockhardt Research Centre D4, M.I.D.C., Chikalthana Aurangabad (MS). Prior to experiment, all the rats were kept at laboratory condition for a period of 10 days for acclimatization. The animals were housed in polypropylene cages under controlled conditions. The animals were maintained under standard managemental conditions and provided with feed and water *ad-libitum* throughout experimental period.

Table 1: Details of Experimental groups of rat

Group Type	Treatment & Dose	No. of Rats	Route
Healthy control	Normal feeding & watering	6	Normal feeding and watering
Acephate Toxicity	*Acephate* @ 34.4 mg/kg Bwt. with vehicle	6	By oral gavage
Plant extract control	*Swertia chirata* aqueous extract @ 100 mg/kg Bwt.	6	By oral gavage
Treatment I	*Acephate* @ 34.4 mg/kg Bwt. with vehicle + *Swertia chirata* aqueous extract @ 50 mg/kg Bwt.	6	By oral gavage
Treatment II	Acephate @ 34.4 mg/kg Bwt. with vehicle + *Swertia chirata* aqueous extract @ 100 mg/kg Bwt.	6	By oral gavage
	Total	30	

3.2 Procurement of material (Acephate and *S. chirata*)

Powder form of *Acephate* was procured from Department of Pesticide, VNMKV College, Parbhani. Dose of *Acephate* was calculated as 1/20th of LD_{50} (688 mg/kg) of male wistar rats [22] *Acephate* powder was weighed and then it was dissolved in 1ml propylene glycol per animal. This solution was used to induce toxicity in male Wistar rats.

Swertia chirata plant was procured from local market of Parbhani (MS) and powered by using electric grinder. Extraction was done by hot water extraction method. The whole plants (stem, leaves and roots) powder @ 250 gm was dissolved in 2 lit. of Distilled water and boiled till it makes a half of it i.e. 1 lit. of this plant solution. After that this solution was poured in a conical flask and cooled down at room temperature. With the help of muslin cloth and whatman filter paper no.42 this solution was filtered in other conical flask and the final *Swertia chirata* plant extraction was obtained to feed to experimental male Wistar rats.

3.3 Relative organ weights

The relative organ weights of liver, kidneys were measured because they are most sensitive toxic substances. Also, weights of Spleen and testes as a reproductive organ of male rats of all experimental groups were recorded at the end of trial.

All the experimental rats from each group were sacrificed by giving high dose of anesthesia and cervical dislocation on 28th day of experimental trial. Organs like liver, kidneys, spleen and testes of experimental rats were separated carefully from the carcass and weighed and weights were expressed in grams (g). Relative organs weights were computed.

3.4 Pathomorphological studies

The rats were sacrificed after completion of 28 days of experiment after recording the gross lesions. The tissue pieces of suitable thickness of liver, kidneys, brain, spleen, intestines, testes, and skin were collected to evaluate microscopic toxico pathological alterations. The collected tissue samples were fixed and preserved in 10 % neutral buffer formalin. After fixation the collected tissue pieces were processed as per the standard procedure. Paraffin embedded tissues were sectioned at 3-5 µ thickness and stained with routine Haematoxylin and Eosin method [6].

4. Results & Discussion

4.1 Pathomorphological Studies

Table 2: Mean values of Body Weight of experimental rats of all the groups at weekly intervals (g/rat/week) of study

Groups of rat	Body weight (gms) Intervals of study						
	0 day	7th day	14th day	21st day	28th day	CD	Statistics
I	^{m}170.83(± 4.01)	^{m}170.33(± 3.71)	^{m}170.50(± 3.50)	^{n}176.33^{a}(± 3.29)	^{n}180.33^{a}(± 2.82)	4.161	S
II	^{m}170.83 (± 2.02)	^{m}172.33(± 2.15)	^{m}170.66(± 1.94)	^{m}168.66^{c}(± 2.15)	^{n}166.50^{c}(± 2.12)	4.161	S
III	^{m}168.00(± 6.68)	^{m}170.50(± 6.30)	^{m}172.33(± 5.57)	^{n}180.50^{b}(± 4.79)	^{o}187.00^{b}(± 4.82)	4.161	S
IV	^{n}170.33(± 2.44)	^{mn}169.33(± 2.44)	^{mn}167.33(± 2.44)	^{mn}166.33^{c}(± 2.44)	^{m}164.50^{c}(± 2.50)	4.161	S
V	^{m}168.33(± 3.75)	^{m}169.16(± 3.60)	^{mn}171.00(± 3.53)	^{n}175.00^{a}(± 3.53)	^{o}180.00^{a}(± 3.23)	4.161	S
CD	-	-	-	4.161	4.161		
Statistics	NS	NS	NS	S	S		

* Means bearing similar superscripts in column and rows do not differ significantly (P< 0.05)

* Superscripts (a b c d) for column and Superscripts (m n o) for rows.

* Values in the parameter is indicate ± S.E.

Table 3: Relative organ weights of experimental male rats at 28th day of experiment

Groups of rat	Relative organ weights at 28th day interval (Mean ± S.E., gms)			
	Liver	Kidney	Spleen	Testes
I	$4.00^{a} \pm 0.07$	2.05 ± 0.03	$0.35^{a} \pm 0.005$	$2.60^{a} \pm 0.02$
II	$2.79^{b} \pm 0.04$	2.08 ± 0.01	$0.10^{c} \pm 0.003$	$1.39^{b} \pm 0.02$
III	$3.89^{a} \pm 0.09$	2.00 ± 0.07	$0.34^{ab} \pm 0.008$	$2.58^{a} \pm 0.05$
IV	$2.55^{b} \pm 0.10$	2.09 ± 0.01	$0.09^{c} \pm 0.003$	$1.36^{b} \pm 0.03$
V	$3.98^{a} \pm 0.10$	2.05 ± 0.02	$0.34^{b} \pm 0.006$	$2.55^{a} \pm 0.03$
CD values	0.257	-	0.016	0.106
Statistics	S	NS	S	S

*****Means bearing similar superscripts in column and rows do not differ significantly ($P < 0.05$)

4.2 Body weights and Relative organ weights

Experimental male rats of healthy control group (Group I) were normal, active and apparently healthy with normal body weight and relative organ weights of rats throughout the period of trial.

In rats of toxicity control group (Group II) fed with acephate @ 34.4 mg/kg Bwt., for 28 days daily P.O. showed prominent clinical signs such as increased salivation, piloerection, lethargy, increased urine output, diarrhoea and hair loss. Body weight was significantly decreased (from 14th day onward) [17]. Reported significant decreased in Body weight. in acephate treated groups of rats at 21st and 28th day of experiment as compared to that of 14th day [11]. Observed the similar clinical signs and consistant reduction in Body weight of rats fed acephate (@ 1000 ppm) after day 8 in 39 days study. Similarly [3], observed reduction in Body weight of male rats treated with high dose of acephate during 4th week of exposure as compare to control group.

Relative organ weights of (Group II) liver, kidney and testes (on 28th day) were significantly decreased, however, kidney weights remain unaltered [21]. Observed significant increase in liver weight of rat in Imidacloprid exposure to wistar rats [10], in Octyphenol (OP) toxicity in male rats [9], in Imidacloprid toxicity in mature male rats were observed significant decreased in testes weight of rat respectively.

In rats of plant control group (Group III) fed with *S. Chirata* were normal, active and apparently healthy throughout the trial. Body weights and relative organ weights of rats of this group were found comaparable to healthy control group. In Ayurveda *S. chirata* is described as easily digestible [12]. It helps in blood purification and immunomodulatory [18] role of amarogentin present in it has been established, which might have help in better improvement of Body weight.

Rats fed with acephate @ 34.4 mg/kg Bwt, and treated with *S. Chirata* (@ 50 mg/kg Bwt.) (Group IV) were lethargic with clinical signs exhibited were piloerection, increased urine output, diarrhoea and hair loss. Body weights were significantly decreased (at 14th day onwards). Relative organ weights of liver, kidney and testes (on 28th day) were significantly decreased, however, kidney weights remain unaltered. The rats of Group V (Treatment II) were normal, active and apparently healthy with normal body weight and relative organ weights of rats throughout the experimental period.

4.3 Gross pathological alterations

In the present study, experimental male Wistar rats treated with ace hate at the end of trial exhibited significant decrease in liver, spleen and testes weights, when compared to respective weights in control Group. Relative organ weights of liver, spleen and testes of rats of group I, III and V did not show any, significant variation amongst them.

The organs of rats of group I, III and V did not show any gross changes. However, rats of group II and group IV had mild to moderate congestion of liver and focal areas of necrosis and kidneys, spleen, Intestines, testes, brain and skin did not showed any appreciable gross changes.

4.4 Histopathological alterations

The histopathological assessment of liver belonging to experimental rats of Acephate toxicated group (Group II) revealed marked congestion of capillaries and congestion of central hepatic vein with extensive and multifocal dilatation of central vein. Dilation and congestion of sinusoidal spaces, Focal areas of cystic degeneration in parenchyma were also evident, Focal areas of degeneration (Granular) and fatty changes in hepatocytes of peri-central area, Diffuse areas of coagulative necrosis (mostly centrilobular) in hepatocytes, with some of the hepatocytes were completely necrosed, Hyperplasia of bile duct and mild proliferation of fibrous connective tissue around hepatic portal triad, and MNC infiltration and thickened capsule of liver (Fig: 1). Similar findings were observed by [14, 3, 21 & 15]. In rats of group IV, congestion of central hepatic vein, multifocal areas of degenerative changes, multifocal areas of fatty changes, focal areas of necrosis in hepatocytes were evident in liver sections. The extent and intensity of histomorphological changes noted in rats of this group were comparatively less than the rats of group II (Fig: 2).

The histo-architectural studies of kidney in experimental rats of Acephate toxicated group (Group II) revealed that, overall architecture was maintained, congestion of capillaries, diffuse interstitial haemorrhages and increased Bowman's space were seen. There were diffuse cellular swelling, vacuolar degeneration, diffuse necrotic changes in tubules and presence of hyaline/ proteinious casts in the tubular lumen with focal MNC infiltration in renal parenchyma. Focal to diffuse cystic degenerative changes, large sized cyst lined by thick fibrous tissue were also observed at places (Place: 3). The patho-morphological changes observed in kidneys of (OP) treated rats reported by [3, 21 & 15], supports the findings of present study. Overall architecture of kidney in rats of group IV showed congestion of capillaries and focal interstitial haemorrhages, at places increased Bowman's space were seen. There were focal areas of cellular swelling, vacuolar degeneration and mild necrotic changes in tubular epithelial cells were evident (Fig: 4).

The spleen of rats of group II (Acephate toxicity) on its histopathology revealed moderate to marked depopulation of lymphocytes from malpighian corpuscles marked congestion of capillaries and marked medullary haemorrhages in sections of spleen (Fig: 5). Similar changes were observed by [17, 3 &15], support this finding. However, [21] did not noted any change in spleen section. In rats of Group IV there was

marked congestion of capillaries with mild depopulation of lymphocytes from malpighian corpuscles of spleen section (Fig: 6).

There was diffuse disruption of top portions of the villi; diffuse desquamation of intestinal epithelium of mucosa, vacuolation in epithelial cells and hyperplasia of epithelium in crypts (Fig: 6). At places, goblet cell hyperplasia was evident. In addition, mild catarrhal exudation with few inflammatory cells was seen in the lumen of intestines of rats of group II were also observed. [21] Observed no appreciable changes in intestines in his study. There were focal areas of disruption of the top villi portions; focal desquamation of intestinal epithelium and hyperplasia of epithelium of crypts (Fig: 7) in sections of intestines of rats in this group II.

The testes of acephate intoxicated rats of group II revealed mild, focal depopulation of spermatogonial cells, degenerative and necrotic changes in seminiferous tubules leading to focal emptying of seminiferous tubules, in seminiferous tubules. There was increased inter-tubular spaces and reduction in the size of few tubules (Fig: 9). Similar findings were also observed by [3, 21 & 15] in different pesticide toxicity in rats. However, [10] did not reveal any apperent morphological changes in testes of rats. The testes of rats of group IV revealed mild, focal depopulation of spermatogonial cells, degenerative changes in seminiferous tubules leading to arrested spermatogenesis in seminiferous tubules. However, tubular structure was compact (Fig: 10).

Histopathological findings in the brain of rats of group II consisted of degenerative changes and vacuolation, severe congestion of capillaries, numerous cystic spaces and infiltration of MNC (Fig: 11). Sections of brain in rats of group IV (Treatment II) showed mild congestion of capillaries, focal to diffuse degenerative changes with focal to multi-focal vacuolations. Similar histoarchitecture changes were also observed by [14, 3, 21 & 15] in OP toxicity of experimental animals.

None section of skin of all rats of all experimental groups revealed any histological changes except for mild hyperkeratosis in section of rat of group II.

The gross lesions were observed in liver in acephate intoxicated rats. However, kidneys, spleen, intestines, testes, brain and skin did not reveal any gross alteration in group I, III and V.

Microscopic lesions noticed in liver, kidneys, spleen, intestines, testes and brain were major and significant type. Lesions followed by other organs suggesting liver, kidneys, spleen, testes and brain happened to be targets of acephate toxicity.

The histopathological studies of various targeted organs of experimental rats of group IV and V at the end of trial did not revealed any appreciable changes except minimal to mind congestion and degenerative changes in liver and congestion of capillaries, focal areas of cellular swelling, vacuolar degeneration and mild necrotic changes in tubular epithelial cells in kidneys, marked congestion of capillaries with mild depopulation of lymphocytes from malpighian corpuscles of spleen, mild to minimal changes in section of intestines, mild degenerative changes in seminiferous tubules leading to arrested spermatogenesis in seminiferous tubules with mild congestion of capillaries, focal to diffuse degenerative Changes with focal to multi-focal vacuolations in brain indicative of restoration of histoarchitecture of studied organs by *Swertia chirata* treatment.

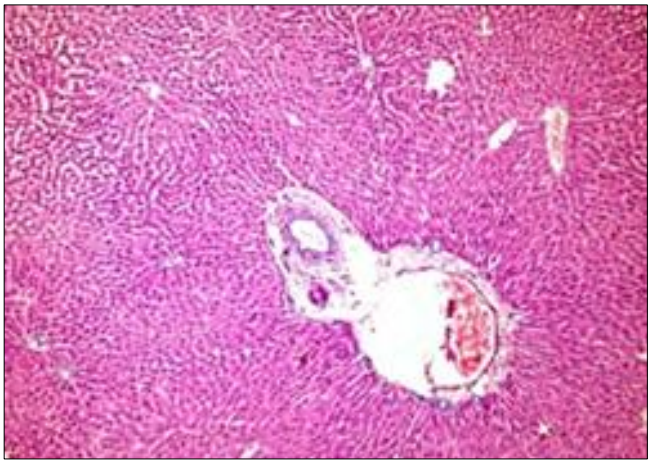

Fig 1: Hyperplasia of bile duct, mild proliferation of FCT around it in a section of liver of a rat of gr. II (H & E X 100) cytoplasmic rarefaction (H & E×400)

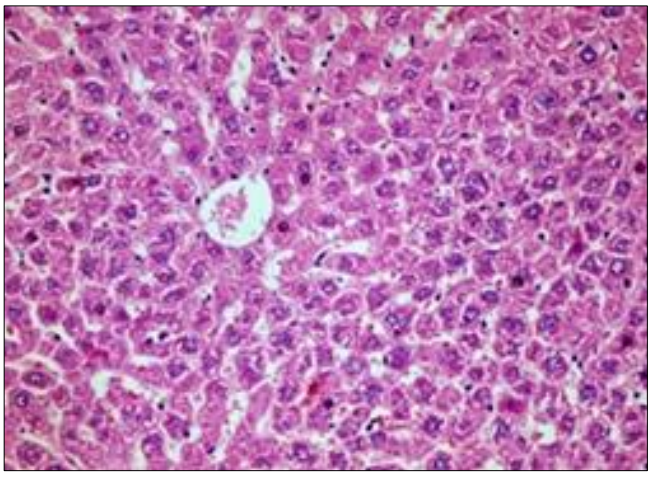

Fig 2: Multifocal areas of degenerative and focal areas of necrotic changes in a liver section of a rat in gr. IV (H & E X 400) 400).space with cytoplasmic rarefaction (H & E×400)

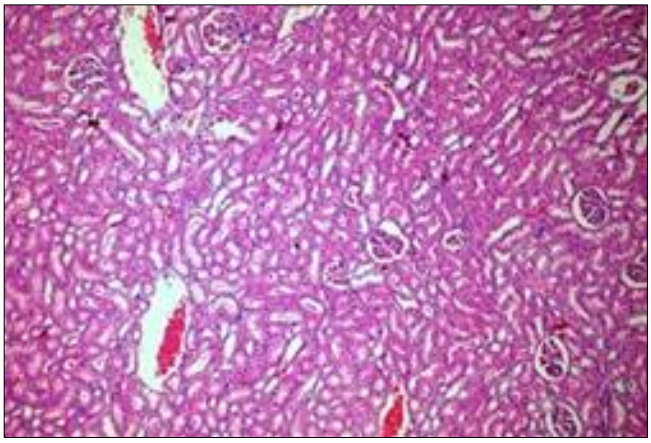

Fig 3: Renal section showing congestion of capillaries and areas of multifocal cystic degenerative changes in a kidney section of rat of gr. II (H & E X 100).

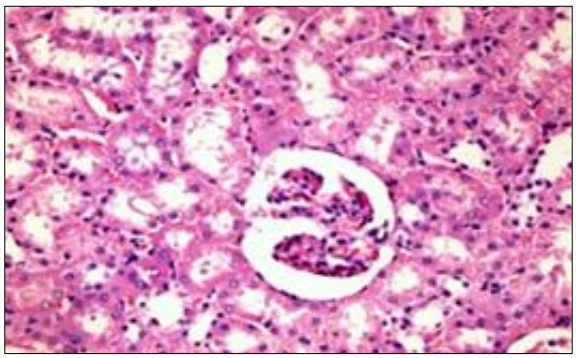

Fig 4: Note increased Bowman's space, degenerative and mild to moderate necrotic changes in tubular epithelial cells in a kidney section of rats of gr. IV (H & E X 400).

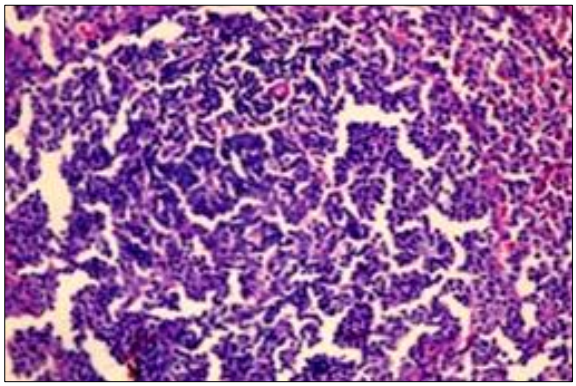

Fig 5: Note marked depopulation of lymphocyte from malphigian corpuscles of spleen of rat of gr. II (H & E X 400).

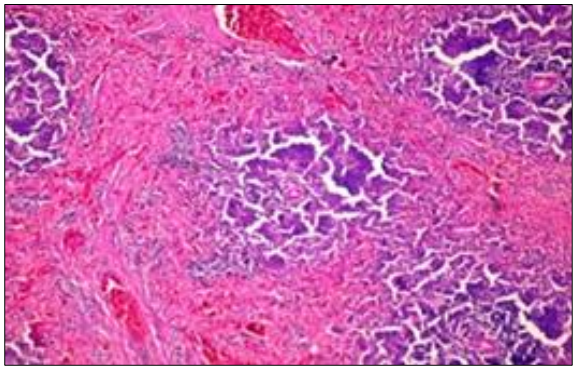

Fig 6: Marked congestion of capillaries with mild to moderate depopulation of lymphocytes from malphigian corpuscle of spleen section of rat of gr. V (H & E X 100).

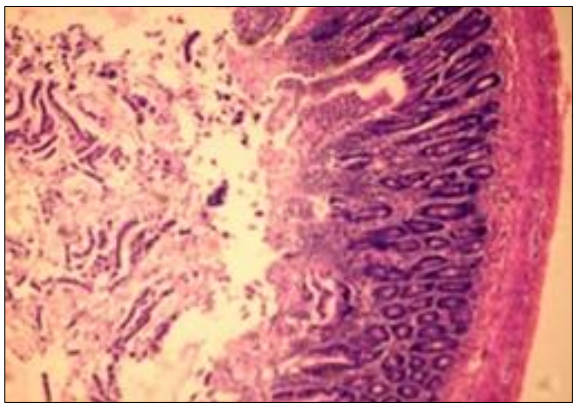

Fig 7: Diffuse areas of disruption of top portions of villi and mild catarrhal exudate with inflammatory cells in the lumen of intestine of a rat of gr. II (H & E X 100).

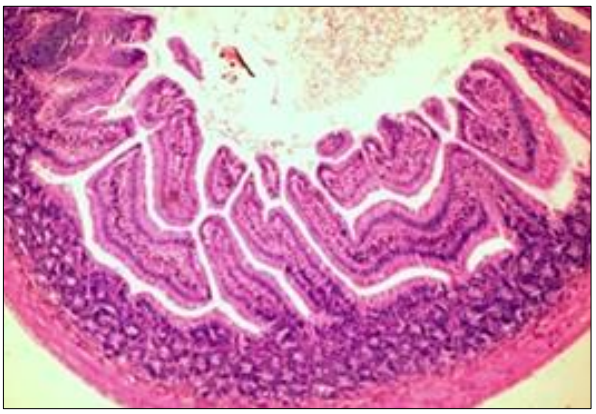

Fig 8: Note focal desquamation of intestinal epithelium and hyperplasia in a rat of gr. IV (H & E X 100).

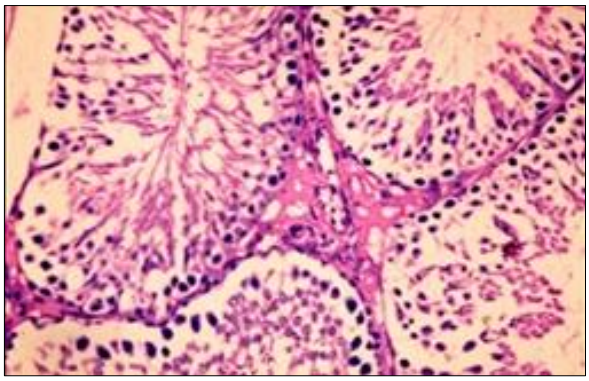

Fig 9: Degenerative and necrotic changes in seminiferous tubules leading to focal emptying of tubules and arrested spermatogenesis in a section of testes of a rat in gr. II (H & E X 400). Spermatogenesis in a section of testes of a rat in gr. II (H & E, X 400).

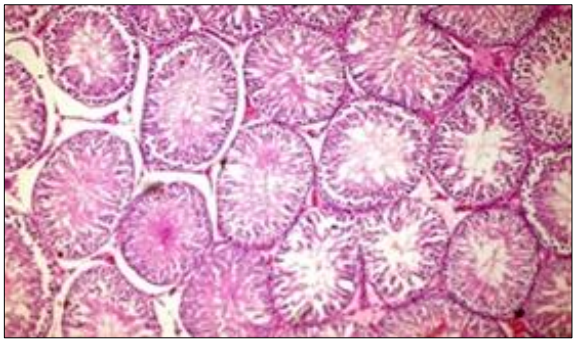

Fig 10: Compact and comparatively better tubular structure of testes in a rat of gr. V (H & E X 100).

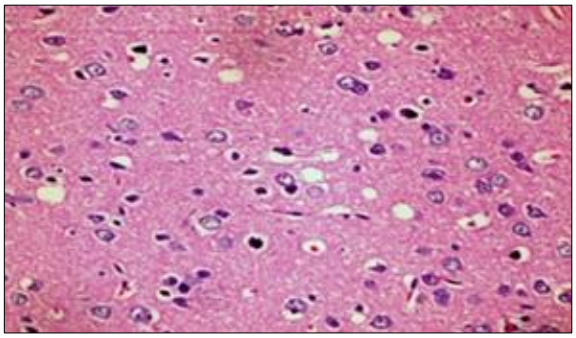

Fig 11: Note severe congestion of capillaries, focal to diffuse degenerative and necrotic changes and vacuolations in neurons of a rat of gr. II (H & E X 100) 100). Cytoplasmic rarefaction (H & E×400)

5. Conclusions

It is concluded that

1. Acephate when given @ 34.4 mg/kg Bwt., by oral gavage with propylene glycol vehicle produced reduction in body weights and significant hepatotoxic, nephrotoxic and moderately neurotoxic effects.
2. On comparison between two treatment groups it was concluded that *S. chirata* @ 100 mg/kg Bwt., had better ameliorative effects than *S. chirata* @ 50 mg/kg Bwt., in subacute toxicity of male wistar rats.

6. Acknowledgements

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7. References

1. Anonymous. The Wealth of lndia" CSIR: New Delhi, 1976, 79 SO.
2. Azmi MA, *et al.* Effect of pesticide residues on health and different enzyme levels in the blood of farm workers from Gadap (rural area) Karachi-Pakistan. Chemo. 2006; 64(10):1739-1744.
3. Bhandaniya AR, *et al.* Toxico-Pathological Studies On Experimentally Induced Acephate Toxicity In Wistar Rats. Wayamda J. of Animal Science. 2012; 4(1):1-8.
4. Bhilave Kulkarni. Response of Organophosphate pesticide Acephate Induced Stress in Biochemical and Haematological Indices of Labio Rohita. Int. J. of Innovative Science, Engineering & Technology. 2015; 2(2):222-226.
5. Costa LG. Current issues in organophosphate toxicology. Clin. Chim. Acta. 2006; 366:1-13.
6. Culling CFA. Handbook of histopathological and his to chemical techniques, 3rd edn., Butterworth and Co. Ltd, 1974, 29-221.
7. Das SC, *et al.* Analgesicandanti-inflammatory activities of ethanolic root extrac to *Swertia chirata* (Gentianaceae). Jordan J. Biol. Sci. 2012; 5:31-36.
8. Du XG, Wang W. Neuroprotective xanthone glycosides from Swertia punicea. J. Nat. Prod. 2010; 73:1422-1426.
9. Golamereza N, *et al.* The effect of Chronic Exposure with Imidacloprid Insecticide on Fertility in Mature Malr Rats. Int. J. of Fertikity and Sterility. 2010; 4(1):9-16.
10. Gregory M, *et al.* Effects of chronic exposure to octylphenol on the male rat reproductive system. Journal of Toxicology and Environmental Health, Part. 2009; 72(23):1553-1560.
11. Gupta PK, Moretto SV. Toxicological studies of monographs and monograph addenda. Oral administration of Acephate in rats J.M.P.R. 2005; 30(3):3-16.
12. Joshi PC, Dhawan V. *Swertia chirata*- an overview. Curr. Sc. 2005; 89(4):635-640.
13. Kirtikar KR, Basu BD. Indian Medicinal Plants, Allahabad. 1984; 3:1664-1666.
14. Laad SN. Toxicity evaluation of acephate, an organic phosphate insecticide B.V.SC. and A.H. thesis, submitted to the COVAS Parbhani, MAFSU Nagpur, 1995.
15. Mishra CS. Studies on Toxico-pathology of Acephate in wistar rats & its Amelioration with cow and goat urine distillates PhD thesis, submitted to the Chhattisgarh Kamdhenu Vishwavidyalaya, Anjora, Durg (C.G.), 2014.
16. Nakuleshwar JD, *et al.* Ameliorative effect of Withania somnifera on acephate administered male albino rats. African. J. Pharmacy and Pharmacology. 2013; 7(23):1554-1559.
17. Sankhala Study on Acephate induced immunotoxicity and its reversal by aqueous extract of Tinospora cordifolia stem in mice. M. V. Sc. Thesis submitted to Anand Agricultural University, Anand, 2007.
18. Scartezzini P, Speroni E. Review on some plants of Indian traditional medicine with anti-oxidative activity. J. Ethnopharmacol. 2000; 71:23-43.
19. Sharma P., and R. Singh Neurotoxic effect of cypermethrin and protective role of resveratrol in wistar rats Uttar Pradesh, India. 2014; 4:104-111.
20. Singh AK, Jiang Y. Immunotoxicity of Acute Acephate Exposure in Control or IL-1-challenged Rats: Correlation between the Immune Cell Composition and Corticosteroid Concentration in Blood. J. Appl. Toxicol. 2002; 22:279-291.
21. Tare RR. Toxicopathhological studies of imadacloprid in wistar rats M.V.SC. thesis, submitted to the COVAS Parbhani, MAFSU Nagpur, 2012.
22. United Phosphorous. Inc. Acephate 97 UP Insecticide, Material data safety sheet, 2010.