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Insufficiency of Kerosine as Solvent to Pyrethroids (Tetramethrin and Permethrin) in the Formulation of Insecticides and its Influence on Blood Parameter in Adult Albino Rats

Maysa M. Thakeb*, Esmat Seif El-Nasr, N. A. Hemeda**, Nadia A. Taha**, Y. L. Awad* and Omyma M. Kandeel*****

**Animal Health Research Institute, **Faculty of Veterinary Medicine, Cairo University and ***Animal Reproduction Department, National Research Centre, Cairo, Egypt.*

THIS INVESTIGATION involved the effect of Kerosine for long time (288 days in these concentrations) as a stress hazardous influence that caused unfavorable manifestations. The direct effect was on hemobiotic system which was concluded from the MCHC and was more indicated in the females than males and that was more clear in the Neutrophiles / lymphocytic ratios.

This investigation showed also the hormonal affection as for the cortisol, testosterone leading to a more hazard insufficiency of the testicular functions.

Thus it is clear that this formulation has a damaging effect on the productive system as well as the haemopoetic system affecting the blood initiating cells as revealed from the peripheral blood studies.

Thus it is necessary to avoid the production of this formulation due to its direct effect on the blood forming system as well as the hormonal profiles in both male and female in individual animals.

Many factors coincide with our environmental derangement that coaless together for the introduction of many pharmaceutical preparations that are needed to combat unacceptable and uneasy invadors which may carry or are the cause of unexpected diseases.

Several components as pyrethroids could be used as being of low toxicity hazards while they could be used to control arthropods.

Kerosine has been reported to control arthropod agricultural pests in 1983, as reported by Teli *et al.* (1983), Kushwaha (1983) in India respectively and Bhowmik, *et al.*(1985) in USA and Arkhipov (1984) in USSR .Also Hofue *et al.* (1987) in Bangladesh in tobacco agriculture.

Kerosine has been found to be non toxic to young children as reported by Deichmann *et al.* (1944) and Foley *et al.* (1954) demonstrated that, following administration of kerosine in a quantity up to 50 ml/kg, and subsequent ligation of the oesophagus, there were no pathological changes in the lungs, intestine or viscera in children.

The inhalation LD_{50} of permethrin in Kerosine in rats was 685 mg /m^3 and the LD_{50} for tetramethrin was 4,640 mg /kg b.wt (Hazelton laboratories Jnc .U.S.A.).

However, Hussein *et al.* (1993) reported on the bad effect of MATOX TM which is an Egyptian commercial insecticide that use Allethrine as an active ingredient and Kerosine as vehicle. They reported that rats exposed to it aerosolically revealed haematological, biochemical and pathological drastic effect.

In this investigation mature albino rats were exposed for long time (288 hours) to aerosolic contamination with Flit which is an Egyptian household insecticide to combat cockroaches.

Materials and Methods

Pyrethroid insecticides

Chemicals used

Flit ™ was obtained from Home Care Co. that consisted of two pyrethroids (0.3% tetramethrin and 0.18% permethrin) with Kerosine as a solvent.

White Kerosine was obtained from Misr Petroleum Co. which is used as a solvent.

Animals and management

A total number of 72 mature albino male (n = 18) and female (n = 54) rats of the Wistar strain obtained from the Animal Health Research Institute Colony were used.

They were 4-8 months of age and with (150 to 200 g. body weight).

Rats were acclimatized to the laboratory conditions for a period of 30 days before being used .The rats were divided into 3 groups , each of 18 females and 6 males, and kept in separate rooms, each of 15.6 m^3 (2.5 m)^3 throughout the experimental period. Rats were fed on a diet (powder) that consisted of crude protein 18.04 %, crude fat 3 %, crude fibres 4 %, vitamins and minerals, and mixed with 10% dried milk (NIDO). Rats were offered food and water ad. Libitum. Water supplied from the water facility used by the Institute.

The rats were exposed to 9 ml /m^3 of normal size from the invaders, Flit ™ (16.2 mg permethrim /m^3 27 mg tetramethrin /m^3 and 9/m^3 ml Kerosine), or Kerosine alone (9 ml / m^3) 6 days a week for 2 months..

* By the end of the exposure rats were sacrificed by decapitation at the morning and during the diestrous of females for examination of the visceral and sexual organs as well as some endocrine glands. Organs weights and histopathology of liver, lung, brain, ovaries, testes, prostate and some endocrine glands of rats were carried out.
* The animals were weighed individually at the beginning and at the end of experiment.
* During-the experimental period, food and water consumption were calculated weekly for each group.

Technique adopted

For haematological examination

PCV (Rommel, 1966), Hb (Vankanpen, 1961), RBCs (Hayem, 1978), Total white cell count (Wintrob, 1971); Differential white cell count (Reich, 1954).

For hormonal and glucose analysis assay

Blood sample were collected without anticoagulant, the radioimmune assay for Cortisol (Hyams and Carey, 1988), for Progesterone (Fuch and Klopper, 1983), for Testosterone (Ten and Jaffe, 1980), for T_4 (Gershengorn *et al.,* 1980) and for glucose (Trender, 1964).

Statistical analysis

Was carried out according to Snedecor and Cochran (1980).

Discussion

A living organism is in a state of continuous interaction with its environment, and tries to maintain the integrity and equilibrium of all kinds of internal regulatory processes even under extreme circumstances which may endanger normal functioning. This may demand an effort from the organism , such processes may be reflected in individual patterns which can give use to specific pathological syndromes. Accordingly, the present study was conducted to determine the effects of common insecticide (Flit™). Clinical symptoms and mortalities, body weight gain, of adults, haemogram and some hormones were studied after 288 hours continuous subjection

Teli *et al.* (1983) used Kerosine for complete killing of Indurabella quadrinataea damaging the Back of Cashew in India. Kushwaha (1983) recommended the use of Kerosine for the management of arthropode-agricultural-pests in India. Bhowmik *et al.* (1985) reported its successful use for Multiflora Rose control in USA. In USS Arkhipov (1984) mentioned the successful application of Kerosine in Male circuit which is a serious pest of potatoes, cucumber, carrot and strawberry.

However, Hussein *et al.* (1993) reported on the bad effect of Matox ™ which is an Egyptian commercial insecticide. In this respect Allethrin was used an active ingredient and Kerosine as vehicle and was experimented on rats. It caused drastic hematological, pathological effects in heart, lung and liver and increased levels of GOT, creatinine, uric acid and blood urea nitrogen.

In Table 1 food and water consumption male and female rats which inhaled Flit^{TM} and in male rats which inhaled Kerosine, was higher than that of controls, whereas these parameters were decreased in females which inhaled Kerosine. This was accompanied with increase in T4 in males while, it decreased in females as seen in Table 5. Lee and Knowles (1965) reported that thyroxine increase the basal metabolic rate. On the other hand, this was accompanied with a decrease in body weight gain. Obviously, insecticides could be described as a stress factor and its response is initiated by the hypothalamus which of course is dependent on its turn on signal processing in higher centers that induce a massive hormonal response. Thus, the increase or decrease in food and water consumption may be due to change in both circulating hormones and a transmitter or modulator in the central nervous system (CNS). Our results agree with that of Nematallah *et al.* (1987) who reported that, body weight is significantly reduced in stressed (immobilized) female rats. Killeen and Rapp (1976) concluded that rats treated with different doses of permethrin showed a small decrease in body weight gain during the first 6 days of treatment, It is seen that this was accompanied with a significant increase in water consumption (Table 1).

TABLE 1. Food efficiency of rat's which inhaled insecticides.

Treatment	Flit TM		Kerosine		Control	
	Sex					
	Female (18)	Male (6)	Female (18)	Male (6)	Female (18)	Male (6)
Food consumption /g/rat /60 days	9310* ↑	8800** ↑	5890** ↓	7090 ↑	8190	5090
Water consumption /ml/rat /60 days	1439.00** ↑	1735.00** ↑	1023.00** ↓	1550.00** ↑	1239.00	1507.00
Beginning weight	147.80± 21.65	174.00± 714.43	167.40± 20.34	211.20± 26.57	160.00± 8.42	190.00± 14.43
Final weight	173.00± 13.51** ↓	225.00± 16.36** ↓	167.60± 15.29*	254.40± 34.56	196.40± 1.98	240.40± 20.41
Weight gain	125.00 ↓	124.00 ↓	136.00	114.00	126.00	125.00
Food conversion /g/rat /60 days	74.48** ↑	70.98** ↑	163.61**	62.19** ↑	65.00	40.72

Results represented: Mean or Mean ± S.E. ( ) (Number of animals)
** P< 0.01
* P< 0.05

Ishmael and Lichfieled (1988) reported a decrease in the body weight of the rats which were exposed to 2500 ppm of Permethrin. In addition, Mickinely *et al.* (1992) recognized that, the amount of water drunk by an animal will be the result of complex neural interactions of regulatory (osmotic pressure and hormones) and non regulatory factors (*e.g.* a state of wellbeing) which determine the avidity of the thirst drive. However, Hiromori *et al.* (1982) found no change in food or water consumption by rats fed tetramethrin for three months.

The present result (Table 2) shows a decrease in M.C.V and increase of M.C.H.C in females which inhaled Flit^{TM} and those with Kerosine showed increase in M.C.V with a decrease in M.C.H and M.C.H.C. In treated males, there was a non significant decrease in PCV, Hb, M.C.V and total RBCs count. Ishmael and Lichfieled (1988) reported that Permethrin up to the concentration of 2500 ppm in diet for 52 weeks in the rats had no effect on the females PCV, HB or total RBCs but in the male 1000 and 2500 ppm affected the clotting factors and the former decreased Hb and PCV values. Shalaby *et al.* (1990) studied the effect of Cyfluthrin as oral administration to pregnant Barki ewes , during the three stages of pregnancy at a dose of 1.3 mg/kg body weight diluted with water 1:150 for five successive days every week. Through each stage of pregnancy they reported a transient decrease in the total erythrocytic and haemoglobin content during all stages of gestation.

TABLE 2. Haematological examination of rats which inhaled insecticide.

Group	Sex	PCV %	Hb (g/dl)	RBCs (million /mm^3)	WBCs (thousands/ mm^3)	M.C.V. (fl)	M.C.H. (Pg)	M.C.H.C. (g/dl)
Flit TM	Female (18)	45.50± 3.08	6.06± 0.04***	5.74± 0.34	9.05± 1.04***	79.27± 2.90**	23.27± 2.90	29.76± 2.60*
	Male (6)	53.00± 5.90	7.20± 1.22	6.70± 0.77	4.45± 0.30	72.22± 2.00	16.00± 1.62	16.90± 2.06
Kerosine	Female (18)	47.36± 1.27	7.36± 0.73*	5.21± 0.66	5.12± 0.43	90.90± 1.10*	14.13± 0.03***	15.54± 0.95**
	Male (6)	54.00± 0.45	8.11± 0.49	6.90± 0.00	5.00± 0.00	71.86± 8.02	12.90± 0.17	15.48± 0.33
Control	Female (18)	49.50± 2.58	10.86± 0.39	5.06± 0.43	4.58± 0.36	85.58± 2.10	21.46± 0.17	21.94± 1.17
	Male (6)	59.00± 0.75	10.13± 5.58	7.61± 0.37	12.20± 8.44	76.62± 2.29	13.43± 1.11	17.39± 0.91

Results represents: Mean ± S.E. ( ) (Number of animals)
Results significantly differ from their control at:
* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$

In this research effort (Table 3) we report an increase in lymphocytes in addition to the decrease of neutrophiles and monocytes in most treated animals. This may be due to the low level of cortisol in the blood of treated animals (Table 5). Meyer *et al.* (1953) reported that there was a clear cut and very marked anti- inflammatory reaction due to the effect of cortisol of the adrenal cortex. Lee and Knowles (1965) reported the same effect of glucocoticoids on lymphocytes. For Table 3, Coles (1986) reported that the excesses of glucocorticoides in animals lead to lymphopenia, leuckocytosis and neutrophilia. Neutophilia due to stimulation of mylopioses in bone marrow.

TABLE 3. Differential leukocytic count (in percentile) of rats which inhaled insecticide

Types of cell / Treatment	Sex	Neutrophiles		Lymphocytes		Monocytes	Eosenophiles	Basophils	Neutrophiles To Lymphocytes
		Unsegmented	Segmented	Large	Small				
Flit ™	Female (18)	3.30± 0.33	1.33± 0.33***	30.33± 7.20*	60.00± 3.80	3.30± 0.33***	1.33± 0.33	1.00± 0.58±	0.07± 0.05***
	Male (6)	2.00± 1.00	2.00± 1.00***	16.67± 4.40	79.00± 4.39**	1.67± 0.33***	0.00± 0.00	0.00± 0.00	0.03± 0.003
Kerosine	Female (18)	1.00± 0.00***	3.60± 1.20***	32.33± 1.45***	60.00± 2.31	2.00± 0.41***	1.60± 0.88	0.00± 0.00	0.02± 0.005***
	Male (6)	1.30± 0.88	10.00± 0.58***	17.00± 6.51	69.00± 7.00	3.33± 1.20	0.67± 0.67	0.00± 0.00	0.14± 0.33
Control	Female (18)	4.00± 0.00	20.50± 0.05	13.00± 0.00	57.00± 0.00	5.00± 0.00	1.00± 0.00	0.00± 0.00	0.36± 0.005
	Male (6)	1.00± 0.00	14.30± 0.03	20.00± 0.00	60.00± 0.00	5.00± 0.00	0.00±0 .00	0.00± 0.00	0.20± 1.50

Results represents: Mean ± S.E. ( ) (Number of animals)
Results significantly differ from their control at:
* P < 0.05
** P < 0.01
*** P < 0.001

TABLE 4. Hormonal assay as recorded from serum analysis of male rats which inhaled insecticide

Treatment	T4 Ng/ml	Cortisol Ng/ml	Testosterone Ng/ml	Glucose g/ l
Flit ™ (6)	2.05±0.28	06.8±0.23	2.59±0.28**	46.62±9.65
Kerosine (6)	2.75±0.33	0.40±0.00*	.53±0.14***	68.36±1.11*
Control (6)	1.65±0.32	2.59±0.64	8.30± 1.13	39.30±9.58

Number of animals ( )
Results represents: Mean ± S.E.
Results significantly differ from their control at:
* P < 0.05
** P < 0.01
*** P < 0.001

TABLE 5. Hormonal assay of serum of female rats which inhaled insecticide.

Treatment	T 4 Ng/ ml	Cortisol Ng/ml	Progesterone Ng/ml	Glucose g/µl
Non pregnant (12) (Flit TM)	1.81±0.40	1.13±0.28	1.04±0.20***	98.27±15.88**
Non pregnant (12) (Kerosine)	1.41±0.50	0.88±0.20*	0.65±0.57***	34.19±3.95
Non pregnant (12) (Control)	3.05±0.78	2.36±0.44	5.56±0.57	31.24±4.20
Non pregnant (10) (Flit TM)	3.57±0.30***	1.41±0.45	1.44±0.38***	58.62±15.46
Non pregnant (10) (Kerosine)	2.13±0.58	1.16±0.18	3.01±1.58***	52.60±13.04
Non pregnant (10) (Control)	1.35±0.13	1.64±0.27	24.77±2.33	77.75±5.30

Number of animals ( )
Results represents: Mean ± S.E.
Results significantly differ from their control at:
* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$

References

Arkhipov, G. E. (1984) The Mole Cricket . *Zashchite- Rastein* **4,** 56-77.

Bhowmik, P.C., Germond , B.J.Sr., Eastman , D.G. and Toung , T. (1985) Multiflora rose control. *Proceedings 39th annual meeting of the northeastern weed - Science,* 219.

Deichmann, W.B., Kitsm, K.W., Wirtherup, B.S. and Johansmann, R.(1944) Kerosine intoxication. *Amer. J. Dis. Child.***83,**466.

Coles, A.H.(1986) "*Veterinary Clinical Pathology*". 4th ed. Churchill Livingston, London, New York, pp. 54-55.

Foley, J. Dreyer, V.B., Soule, B.A. and Woll, K. (1954) Kerosine poisoning in young children . *Radiology,* **62,** 817.

Fuch, S.F. and Klopper, A. (1983)*"Endocrinology of Pregnancy"*. Harper and Row, Hagerstown.

Gershengorn, M.C. Glinoer, D. and Robbin`s , J. (1980) *"Transport and Metabolism of Thyroid Hormones"*. Thyroid gland, M. Devisscher, (New York: Roven Press 1) pp. 81-121.

Hiromori , T., Hosokawa, S., Okuno, X., Seki, T. Suzuki, T. and MiYamoto, J. (1982) Mammalian toxicity of d-isomers of phthalthrin (Neopynamine) fort. *Pharmacometrics* **24,** 179-200.

Hussein , Y.A., El-Ashmawy, I.M. and EL-Swak, A.A. (1993) Effects of exposure to pyrethroid insecticide repellent (MATOX) on albino rats. *Egyptian Journal of Comparative Pathology and Clinical Pathology*, **6** (1), 175-188.

Hofue , M.E., Islami , H.G. and Muzer, S.H. (1987) Effect of plant growth , regulation on the control of tobacco (Nicotinine tabecum). *Bangladesh J. of Agriculture*, **12** (2), 95-102.

Hayem, G. (1978) Researcher sur L`evolution des trematies dans le sang de l` hommeet des vertebras. *Arch. De physiol.*, **5,** p. 692.

Hyams, J.S. and Carey, D.E. (1988) Corticosteroids and growth. *J. Pediatr.*, **113,** 249-254.

Ishmael, V. and Lichfieled , M.M.(1988) Chronic toxicity and carcinogens of permethrin in rats and mice. *Fundmental and Applied Toxicology* **11,** 308-322.

Kassem , R.V. (1972) "*Basic Physiology of Endocrine System* ". Published Union Book Center , Cairo , Egypt .

Killeen, V.C. and Rapp, V.P. (1976) A three month oral toxicity study of F.M.C. 33297 in rats (Bio-Dynamics Inc Project) unpublished report submitted to WHO by EM corporation.Cited in Environmental Health Criteria 94 World Health Organization. Geniva, 1991, p. 69.

Kushwaha, K.S. (1983) Some practical recommendation depicting research highlights in pest management in Rajasthan. *Pesticides* **17**(7), 9-18(b).

Lee, I. and Knowles, F.G. (1965) "*Animal Hormones*". 1st ed. Hutchinson Univ. Library London.

Maysa, Mohammed Thakeb (1996) Effect of some environmental stressors on growth development and behavior of experimental animals.*Thesis presented to Fac. Vet. Med.* Cairo Univ. for pH. D. Vet. (Physiology).

Meyer, R.K., Stucki, V.C. and Ausli Brook, K.A. (1953) An international symposium on aldosterone. edit by Muller , A.F. and O`Conner, C.M. (1958) Churchill LTD, London .

Mickinely, M.J. Oldfield B.J. and Vivas, L. (1992) Osmotic and hormonal regulation of thirst in domestic animals. *Domestic Ani. Endo.* 9-11.

Nematallah , B.R. Dougbag, A., Fatouh, I. and Mohammed , M.M. (1987) Stress effects on morphological and biochemical changes following induced decidulization in rat uteri. *Assiut Vet. Med. J.* **18** (36), 65-73.

Reich, C. (1954) Modified Reight Stain. *Ann. J. Clin. Path.* **24 ,** 881.

Rommel, W. (1966) *Laboratory techniques in veterinary medicine* The laboratory for feeding Hygiene.164 Leipzig, S.Hirze, IM.**27,**55.

Shalaby, S.I.A., Souphy, H. and Abdel Rasek, A.M.A.(1990) Influence of Baythroid insecticide (Cyfluthrin) on haemogram of pregnant Barki ewes. *4th Sci. Cong., Fac. Vet. Med.*, Assiut Univ. pp. 194-201.

Snedecor , G.W. and Cochran, W.G. (1980)*"Statistical Methods".7th* ed. Ames Iowa State University Press, Iowa, USA.

Teli, V.S. , Ambekar , J.S. and Chandele , A.G. (1983) Chemical control of bark-eating caterpillar , Inderbela quadrinotate Walker in cashewnut. *Pestisides* **17** (6), 20-21.

Ten, S.S. and Jaffe, R.B. (1980) Determination of plasma testesterone hormone by radioimmunassay technique. *Technique Reproductive Endocrinol Org. W.B. Standard.* (1978).

Trender, P. (1964) Calorimetric determination of glucose. *Ann. Clin. Biochem.* **6**, 24.

Vankanpen, E.T. (1961) Calorimetric determination of hemoglobin. *Clin . Chem. Acta.* **6,** 538-544.

Wintrob, M.M. (1971) Macroscopic examination of blood. *Am . J. Med. Sci.* **185,** 58.

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عدم كفاءة الكيروسين كمذيب للمركبات البيريثرويد (النترامييثرين واليروميثرين) في تحضير المبيدات المنزلية من خلال تأثيرها الضار على مؤشرات الدم فى الفئران الانجليزية البيضاء

مايسة محمود ثاقب* ، عصمت سيف النصر** ، نبيل احمد طه** ، يوسف لبيب عوض* و اميمة محمد قنديل***
* معهد بحوث صحة الحيوان ** كلية الطب البيطرى – جامعة القاهرة
و***المركز القومى للبحوث– القاهرة – مصر.

يستعمل الكيروسين كمذيب عضوى للمركبات البيروثريدية وبالرغم من استعماله كمبيد حشرى للآفات البيولوجية الزراعية عالمياً وعدم تعرض المنـزل لسمية الكيروسين بصفة عامة فلا يستعمل كمذيب للمركبات الوراثية فى مصر فى بعض المستحضرات المنزلية وقد ثبت أثر الكيروسين نفسه كمذيب عضوى للمستحضر المركب الفلت .

وتعتبر المركبات البيروثريدية اهم المصادر الكيميائية لانتاج المبيدات الحشرية. وقد سجلت اعراض مرضية على حيوانات تجارب باستخدام (الايزالو) المحتوى على البيريثرودية في الكيروسين ولذا تم عمل تجربة بحثية فى هذا المجال باستخدام المركب (الفلت) حيث ادرج (الفلت) كمنتج دوائى لاستعماله كمبيد حشرى منزلى لمقاومة الصراصير – كأفة منزلية

ولذا شملت الدراسة المركب (الفلت) بالصورة المتكافئة على حيوانات تجارب على الفئران البيضاء الكبيرة في اماكن محفوظة لتعرضها للتلوث الهوائى من هذا المركب والكيروسين كعامل اذابة للمستحضر وتم عمل ذلك في مجال هوائي متجانس على عدد ١٨ فأر انجليزى كبير وعدد ٥٤ انثى بالغة قسمت الى ثلاثة مجموعات بتعرضها للكيروسين والمركب المستخدم ومجموعة ضابطة حيث تم التعرض لعدد ٢٨٨ ساعة خلال ستة ايام اسبوعيا بصفة متتالية لبيان اثر التلوث الهوائى على صحة حيوان التجارب المستعمل.

تأثرت كل من المجموعات المعاملة بالكيروسين المستخدم والمركب ولم تتأثر المجموعات الضابطة التى تم دراستها ومقارنتها احصائيا مع كل مؤثر ومدى معنويتها .

تأثر معامل التحول الغذائى فى كل من الذكور والاناث لكل فأر بعد استعماله لمدة ستين يوما.

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