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Teratogenic effects of abamectin in rats

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SUMMARY

The teratogenic effects of abamectin pesticide on pregnant rats were studied following oral administration of 2.85, 1.42 and 0.72 mg/ Kg bw (1/10, 1/20 and 1/40 of the oral LD_{50}, respectively) during the organogenesis period. Treatment with abamectin did not influence the reproductive status (number of uterine implants, resorptions, live and dead fetuses per litter) at all dosage levels. However, it caused significant increase in the percentages of morphological, visceral and skeletal malformations in rat fetuses on exposure to the two high doses compared to control. In addition, abamectin induced different pathological alterations in the placentae and fetal organs in a dose - related manner.

Keywords: Abamectin, teratogenic, fetuses, placenta, malformations, rat.

INTRODUCTION

Abamectin is a broad spectrum insecticide and acaricide. It is used to control insect and mite pests of livestock, crops, ornamental plants and turf and at household, commercial and industrial use areas (U.S. EPA, 2004). It is an oral broad spectrum antiparasitic solution for the treatment and control of abamectin sensitive strains of round worms in sheep, nasal bot and itch mite of sheep and lambs (Norbrook Laboratories, 2005). Also, it is highly effective against gastrointestinal parasites in horses (Mahfooz et al., 2008).

Abamectin is a macrocyclic lactone product derived from the soil microorganism Streptomyces avermitils. It is a mixture of avermectins containing about 80% avermectin B1a and 20% avermectin B1b. Laboratory animals' experiments showed that ingested

avermectin B_{1a} is absorbed into the blood stream by mammals and is rapidly eliminated from the body within 2 days via the feces (U.S. EPA, 1990). Orally administered abamectin elicit a dose-dependent CNS effects, including tremors and ataxia. The sensitivity as well as doses required to produce neurotoxic effects vary from rodents to primates by a 20-fold factor as rodents are more sensitive than primates (U.S. EPA, 1994). Abamectin has neurotoxic effects by stimulating the release of gamma-aminobutyric acid and increasing in chloride ion influx causing paralysis and death (European Food Safety Authority, 2008).

Most reports on the fetotoxic and teratogenic potential of abamectin in mice and rabbit were only at the maternally toxic doses (Gordon et al., 1985; Lankas and Gordon, 1989; Hurtt et al., 2003; European Food Safety Authority, 2008 and U.S EPA, 2008).

Few studies recorded some external, visceral and skeletal fetal anomalies in rat's offsprings exposed in utero to abamectin (dams treated orally with abamectin at dosage levels of 0.4, 0.8 or 1.6 mg/kg bw/day on days 6 through 19 of gestation) (Gordon et al., 1982a; U.S. EPA, 2004 and European Food Safety Authority, 2008). Other studies showed no evidence of embryo/fetotoxicity or teratogenicity at any of the oral dosage levels 0.25, 0.5 or 1.0 mg/kg bw/day of the delta 8, 9-isomers of abamectin when given to pregnant rats on days 6 through 17 of gestation (Gordon et al., 1987a).

Therefore, the aim of the present study is to investigate the teratogenic potential of abamectin pesticide on pregnant rats following oral administration of different none maternally toxic doses (1/10, 1/20 and 1/40 of the oral LD_{50}) during the organogenesis period ($6\text{-}15^{th}$ days of gestation).

MATERIALS AND METHODS

1. Animals:

Thirty six sexually mature male and female Sprague-Dawley rats (180-200 g) were used as lab animals in this study. Upon arrival, the males and females were housed separately in metallic boxes with *ad libitum* access to clean tap water and balanced ration. Sixteen mature healthy male and female albino rats were used for determination of the acute oral LD_{50} of abamectin. In addition, a total of twenty pregnant females were used in teratogenicity investigation.

2. Experimental design:

Abamectin 1.8 % emulsifiable concentrate (EC, Sigma- Aldrich Co, Saint Luis, USA) containing averemectin $B1_a$: $C_{48}H_{72}O_{14}$ (MWt: 872.1Dalton); averemectin $B1_b$: $C_{47}H_{70}O_{14}$ (MWt: 858.1 Dalton) was used in this study.

Determination of the acute oral LD_{50} of formulated abamectin was done according to Weil (1952), then 1/10, 1/20 and 1/40 of the oral LD50, were used in the teratogenicity investigation. Pregnant females were divided into four equal groups (five animals for each). The first group (A1) administered distilled water orally on days 6 - 15 of gestation (organogenesis period) and served as control. The other 3 groups A2, A3 and A4 were administered abamectin orally during organogenesis period at 2.85, 1.42 and 0.72 mg/ Kg bw (1/10, 1/20, 1/40 of the oral LD_{50}, respectively).

3. Scheduled time and procedures of teratological examination:

Teratological examination was done according to Manson and Kang (1994). All treated and control female groups were sacrificed under gaseous anesthetic chloroform at 20th day of gestation. The number of implantation and resorption sites, live and dead fetuses were counted. The fetuses and placentae were weighed and examined for gross external abnormalities. One fetus and one placenta/litter were used for histopathological examination. The remained fetuses were divided into one third kept in Bouin's fixative for at least one week, after which, fetuses were sectioned using Wilson's free-hand razor blade sectioning technique searching for internal visceral malformations. The other two thirds were kept in ethanol for subsequent preparation for skeletal examination.

4. Histopathological investigation:

The fetuses and placentae intended for histopathological investigation were fixed in 10% neutral formalin and prepared for examination according to Bancroft et al. (1996).

5. Statistical Analysis:

Values are given as percentages and mean ± standard error (SE). Statistical significances of treatment effects of abamectin on fetal and placental weights were determined by one way ANOVA. Chi square test was used for the comparison of the different morphological, visceral and skeletal anomalies between treated and control groups (SPSS: statistical package for social sciences 10.0 for windows) (Alan and Duncan, 2001).

RESULTS

1. The acute oral LD_{50} of abamectin

The calculated acute oral LD_{50} of abamectin based on the mortality data (recorded during 24 hours) in rats orally received different doses of abamectin (Table 1) was 28.538 mg/kg bw. Symptoms of intoxication were observed few hours after administration including: Severe generalized tremors arched back and stretched head in some rats. Others showed salivation, mydriases, bulging of eye balls, comatose and dullness of the eyes before death.

Table (1): Mortality data of the different acute oral doses of abamectin in rats

Group	Dose (mg/kg bw)	No. of dead animals	No. of living animals
1	96	4	0
2	48	3	1
3	24	2	2
4	12	0	4

2. Results of teratogenicity investigations:

The abamectin - induced morphological changes are recorded in Table (2). Abamectin at all doses (A2, A3, and A4 treated groups) produced insignificant elevation in the percentages of early resorptions (Fig. 1) compared to the control (A1). The percentages of the live fetuses were insignificantly decreased in A2, A3, and A4 treated groups compared with control. The mean fetal body weights were significantly reduced in all treated groups compared with the control group. The mean placental weights were significantly lower in A2 and A3 treated groups, however it was insignificantly lower in A4 treated group. The percentages of the dwarf fetuses were significantly increased in A2 (Fig. 2) and A3, treated groups and was insignificantly increased in A4 treated group. The percentages of fetuses that had s/c hemorrhage in A2, A3 and A4 treated groups were insignificantly increased comparing to that recorded in control (Fig. 3). The most prominent visceral abnormalities in the examined fetuses were found in nares, eyes, brain, heart, lung, chest and kidneys (Table 3). Abamectin in A2 and A3 treated groups produced significant elevation in the percentages of rat fetuses that had malformations in these organs except nares in group A2 and nares and heart in group A3 compared with that recorded in the control group. In A2 treated group the observed abnormalities were in the form of dilated nares, and/or microphthalmia, dilated brain ventricles, hypertrophy of the heart, hypoplasia of the lung, intrathoracic hemorrhages and dilated renal pelvis. However, in A3 treated group, there were dilated nares (Fig. 4), microphthalmia, dilated brain lateral ventricles (Fig. 5), hypertrophy of the heart (Fig. 6), hypoplasia of the lung (Fig. 6), intrathoracic hemorrhages (Fig. 6) and dilated renal pelvis (Fig. 7). Abamectin in A4 treated group produced insignificant elevation in the percentages of rat fetuses that had malformations in the examined visceral organs except in dilated renal pelvis (significant elevation) compared with that recorded in the control group.

Many skeletal abnormalities in the examined fetuses were recorded in skull bones, sternum,

ribs, phalanges, sacral vertebrae and caudal vertebrae on organogenesis period exposure (Table 4). Abamectin in A2 and A3 treated groups produced significant elevation in the percentages of rat fetuses that had skeletal malformations except in sacral vertebrae (in group A2) and wide open fontanel and sacral vertebrae (in group A3) compared with that recorded in control. The recorded skeletal abnormalities in A2 group were wide open fontanel, incomplete ossification of parietal and interparietal bones, sternum (reduction in the number, hypoplasia or even complete absence of sternbrae), wavy or short last ribs, reduction in the number or even complete absence of phalanges, and/or sacral vertebrae and absence of caudal vertebrae. However, the skeletal abnormalities in A3 group, were wide open fontanel, incomplete ossification of parietal and interparietal bones (Fig. 8), sternum (reduction in the number, hypoplasia or even complete absence of sternbrae) (Fig. 9, 10), wavy or short ribs, reduction in the number or even complete absence of phalanges, absence of sacral and caudal vertebrae (Fig. 11). Abamectin in A4 treated group produced insignificant elevation in the percentages of rat fetuses that had skeletal malformations compared with that recorded in control.

Table 2. Morphological examination of rat fetuses obtained from control and treated dams at days 6-15 of gestation

Group \ Parameter	No. of pregnant dams	No. of uterine implants	Early resorption sites		Late resorption sites		Live fetuses		Mean fetal weights by g.	Mean placental weights by g.	External morphological abnormalities			
											Dwarfism		S/c Hemorrhage	
			No.	%	No.	%	No.	%			No.	%	No.	%
A1(control)	5	53	1	1.88	0	0	52	98.1	4.85 ± 0.04	0.76 ± 0.02	1	1.9	0	0
A2 (2.85 mg/kg b.w abamectin)	5	47	2	4.25	0	0	45	95.7	3.52 ± 0.09*	0.60 ± 0.02*	25	55.5*	2	2.4
A3 (1.42 mg/kg b.w abamectin)	5	51	2	3.92	0	0	49	96.1	3.80 ± 0.06*	0.63 ± 0.02*	22	44.9*	1	2.04
A4 (0.71 mg/kg b.w abamectin)	5	51	2	3.92	0	0	49	96.1	4.46 ± 0.07*	0.72 ± 0.02	3	6.10	1	2.04

Data are presented as mean ± standard error unless otherwise stated.

*: Significant difference between treated and control groups at $p \leq 0.05$

Table 3. Visceral malformations of rat fetuses obtained from control and treated dams at days 6-15 of gestation

Group / Parameter	No. of examined fetuses	Malformations of													
		Head						Chest						Pelvis	
		Nares		Eyes		Brain		Heart		Lung		Intrathoracic hemorrhages		Kidneys	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A1 (control)	16	1	6.2	0	0	0	0	0	0	0	0	1	6.2	0	0
A2 (2.85 mg/kg b.w abamectin)	14	3	21.4	4	28.6*	7	50*	4	28.6*	6	42.8*	6	42.8*	0	0
A3 (1.42 mg/kg b.w abamectin)	15	2	13.3	4	26.6*	7	46.6*	3	20	5	33.3*	6	40.0*	7	50*
A4 (0.71 mg/kg b.w abamectin)	15	1	6.6	1	6.6	3	20	1	6.6	3	20	4	26.6	7	46.6*
														4	26.6*

Data are presented as percentages of viscerally deformed fetuses in relation to total number of examined fetuses

*: Significant difference between treated and control groups at $p \leq 0.0$

Table 4. Skeletal malformations of rat fetuses obtained from control and treated dams at days 6-15 of gestation

Group / Parameter	No. of examined fetuses	Malformations of													
		Skull Bones				Sternum		Ribs		Phalanges		Sacral vertebrae		Caudal vertebrae	
		Wide open fontanel		Incomplete ossification of parietal and/or interparietal bones											
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No	%
A1 (control)	31	1	3.2	0	0	1	3.2	1	3.2	1	3.2	0	0	1	3.2
A2 (2.85 mg/kg b.w abamectin)	26	9	34.6*	10	38.5*	20	76.9*	8	30.7*	10	38.5*	3	11.5	14	53.8*
A3 (1.42 mg/kg b.w abamectin)	29	5	17.2	7	24.1*	22	75.8*	7	24.1*	9	31.0*	1	3.4	13	44.8*
A4 (0.71 mg/kg b.w abamectin)	29	1	3.4	1	3.4	2	6.9	1	3.4	1	3.4	0	0	2	6.9

Data are presented as percentages of skeletal deformed fetuses in relation to total number of examined fetuses

*: Significant difference between treated and control groups at $p \leq 0.05$

4. Results of histopathological examination:

Abamectin exposure resulted in different pathological alterations in the placentae and fetal organs in a dose - related manner. Cellular necrosis and desquamation of chorionic villi epithelia of placenta (Fig. 12) was recorded.

The fetal brain showed demylination of nerve fibers. Cerebrum neuronal cells had pyknotic nuclei and vacuolated cytoplasm (Fig. 13). Hemorrhage and congestion in the heart with vacuolated myocardial cells and loss of longitudinal and cross striations was seen (Fig. 14). The lung showed congestion of blood vessels and alveolar walls, perivascular edema, alveolar congestion, pyknotic nuclei and vacuolation of alveolar lining epithelia (Fig. 15). There was sinusoidal congestion, hydropic degeneration of hepatocytes (Fig. 16). Pancreas showed interstitial edema, loss of zymogen granules and pyknotic nuclei in pancreatic cells. The islets of langerhans were congested with reduced size due to cell necrosis (Fig. 17). Necrobiotic changes were observed in the kidney in the form of granular cytoplasm, pyknotic nuclei, vacuolation of tubular epithelia; cloudy swelling in tubular cells of proximal convoluted tubules with complete destruction of some cells. The glomeruli were congested with hyper cellularity and narrowing of Bowman's space (Fig. 18).

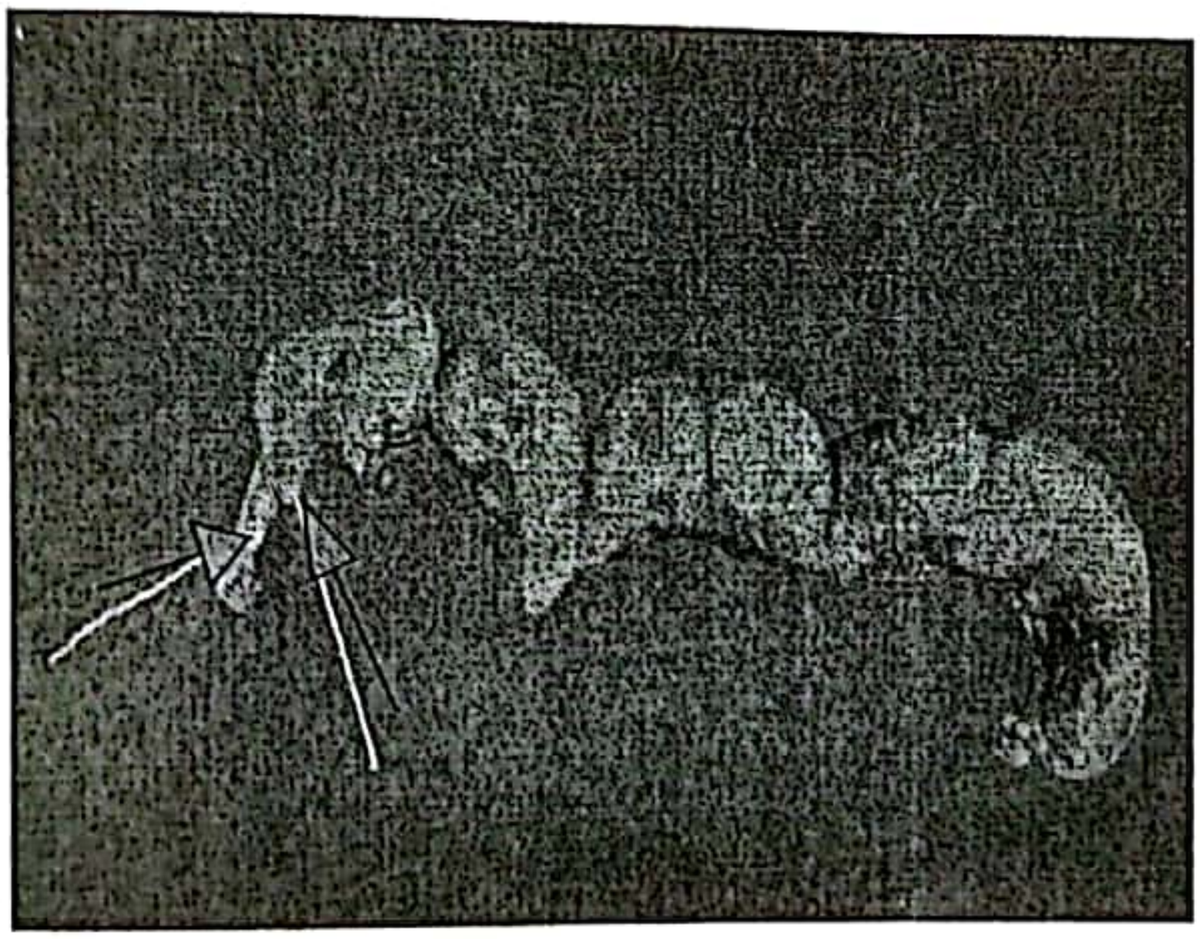

Fig. (1): Uterus of a pregnant rat treated orally with 2.85 mg/kg bw (1/10 LD_{50}) abamectin on days 6-15 of gestation (organogenesis period) showing two early resorption sites in the left horn.

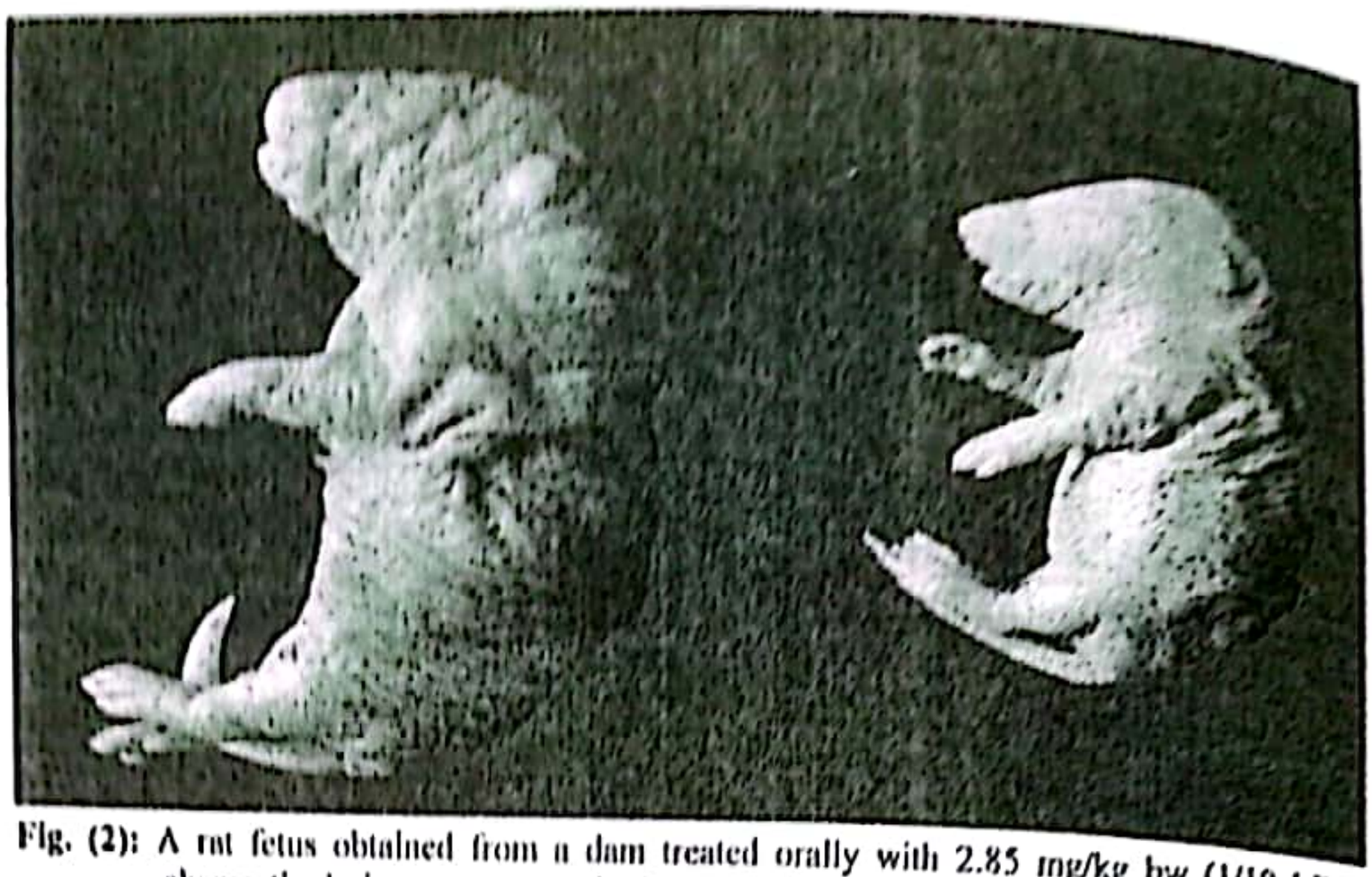

Fig. (2): A rat fetus obtained from a dam treated orally with 2.85 mg/kg bw (1/10 LD_{50}) abamectin during organogenesis showing dwarfism (right) and a control one (left).

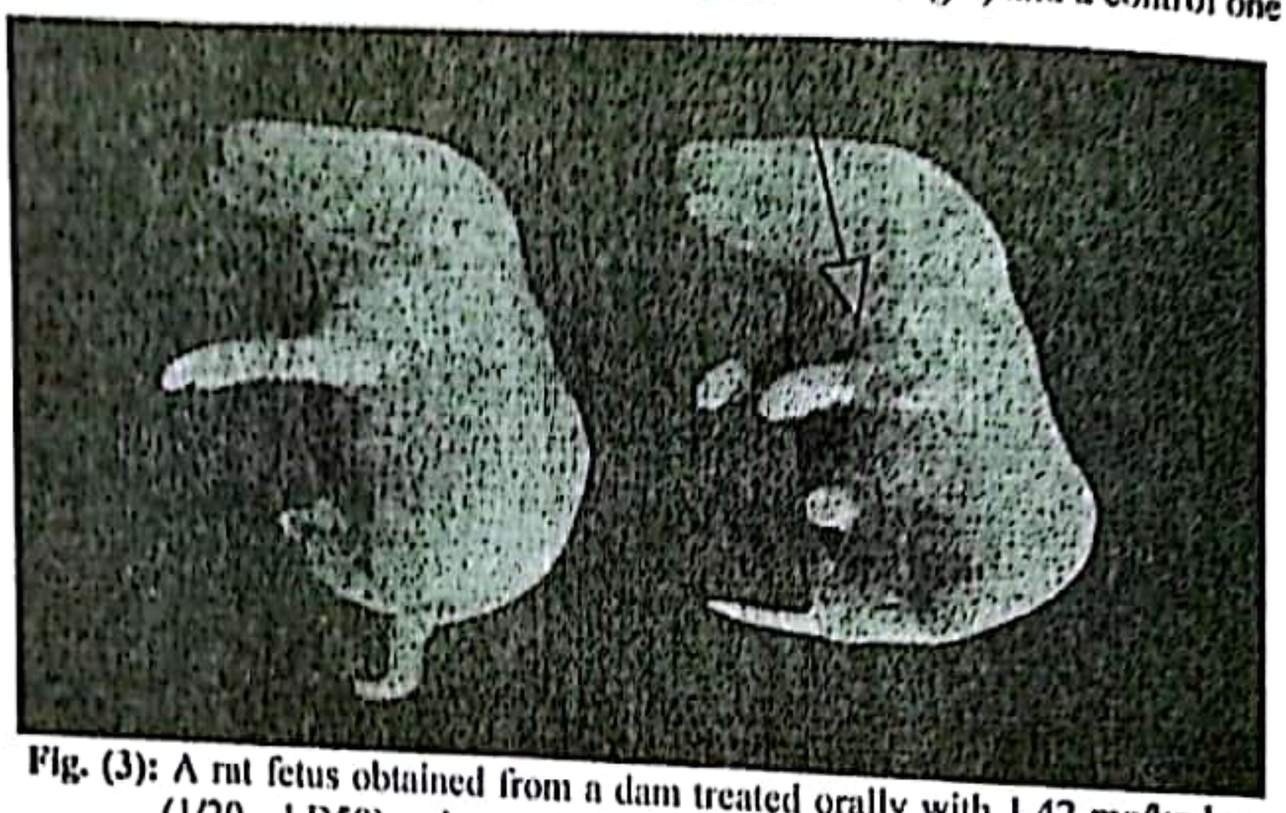

Fig. (3): A rat fetus obtained from a dam treated orally with 1.42 mg/kg bw (1/20 LD50) abamectin during organogenesis showing s/c hemorrhage at elbow joint (right) and a control one (left).

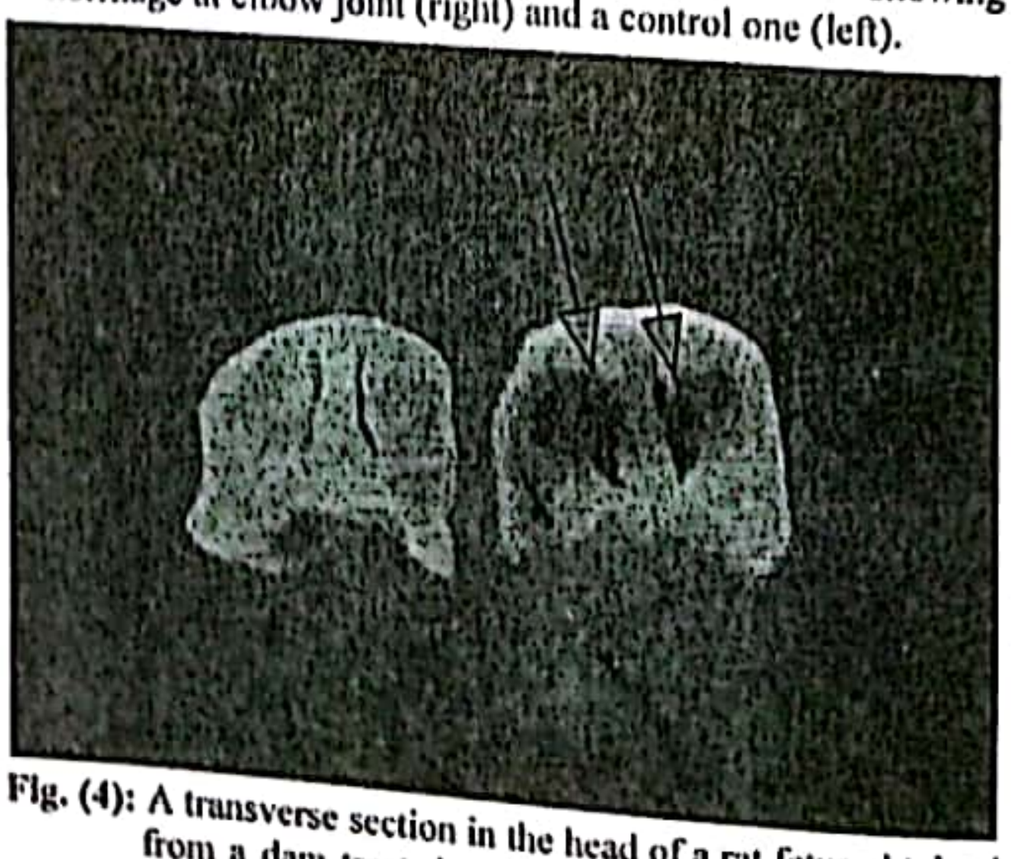

Fig. (4): A transverse section in the head of a rat fetus obtained from a dam treated orally with 1.42 mg/kg bw (1/20 LD50) abamectin during organogenesis showing dilated nares (right) and a control one (left).

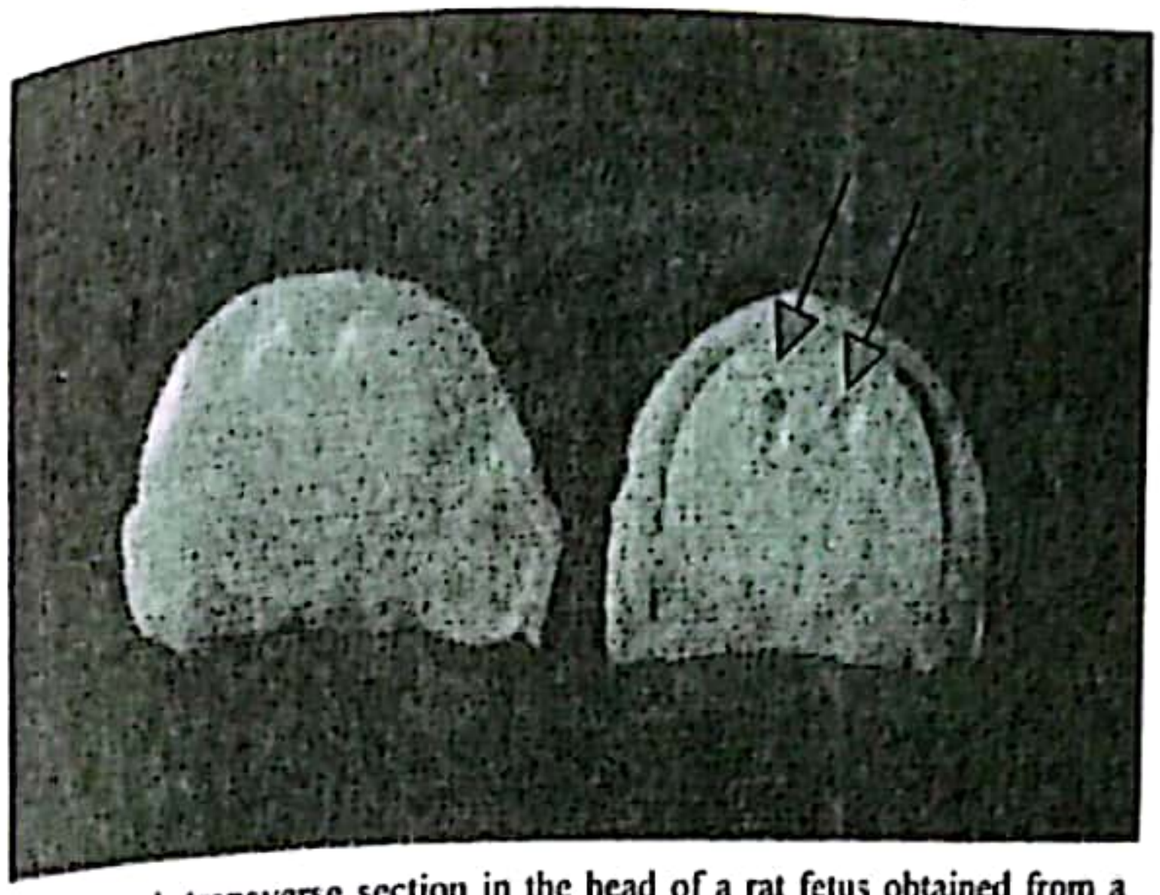

Fig. (5): A transverse section in the head of a rat fetus obtained from a dam treated orally with 1.42 mg/kg bw (1/20 LD50) aba9mectin during organogenesis showing moderate dilatation of brain lateral ventricles (right) and a control one (left).

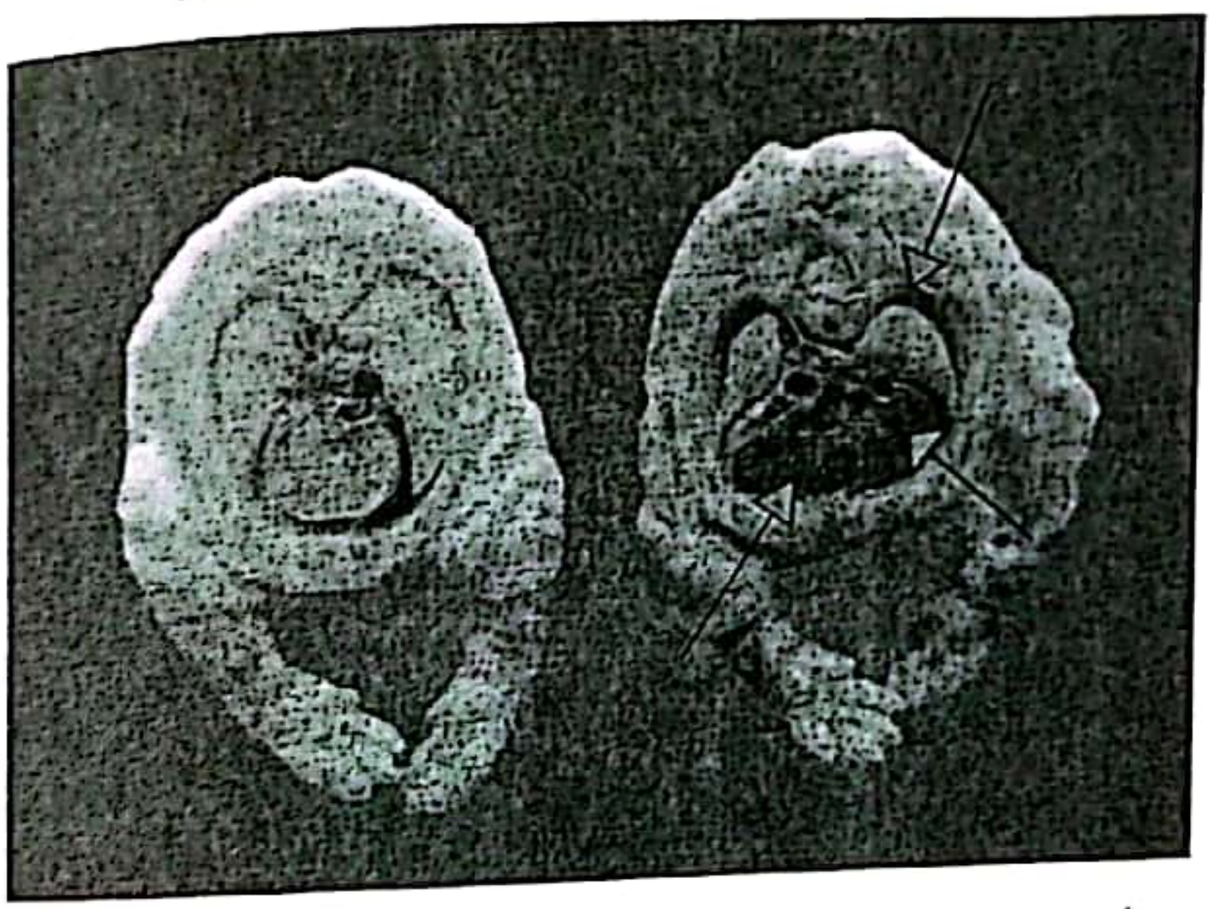

Fig. (6): A transverse section in the chest of a rat fetus obtained from a dam treated orally with 1.42 mg/kg bw (1/20 LD50) abamectin during organogenesis showing intrathoracic hemorrhage, hypertrophy of the heart and hypoplasia of the lung (right) and a control one (left).

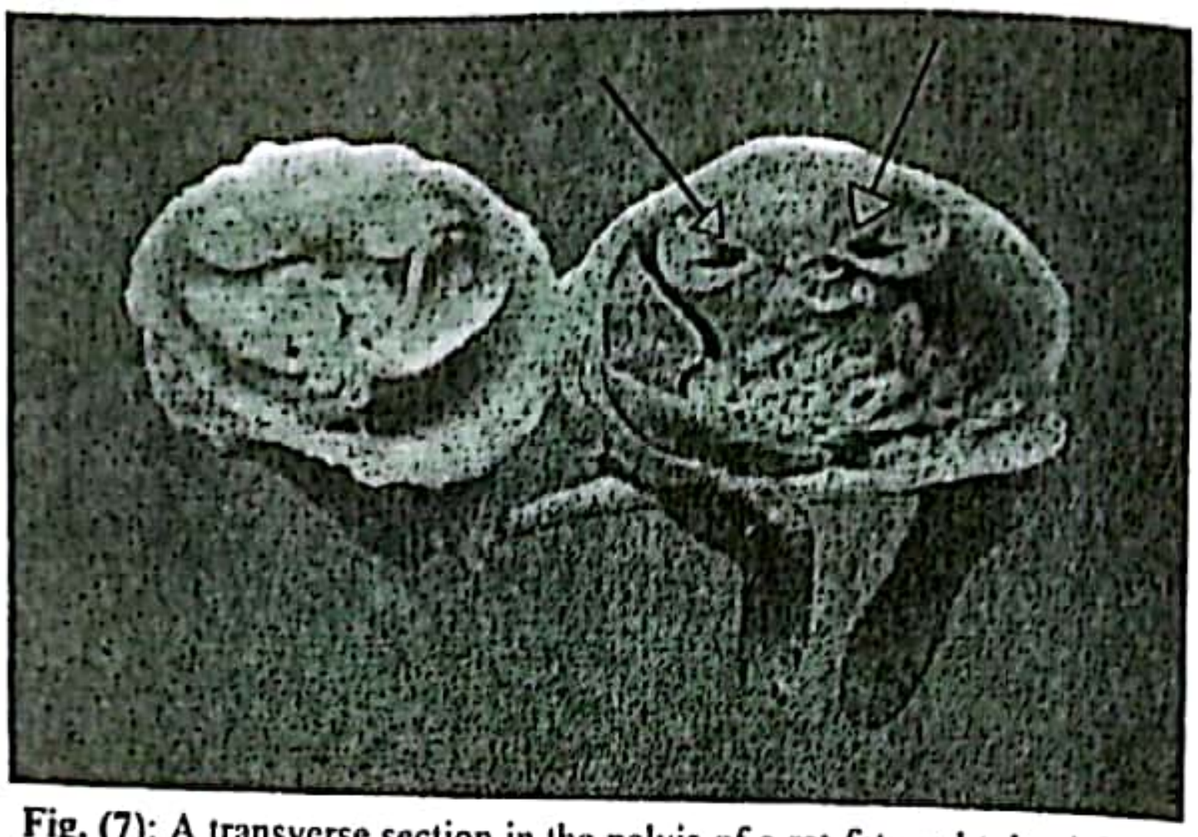

Fig. (7): A transverse section in the pelvis of a rat fetus obtained from a dam treated orally with 1.42 mg/kg bw (1/20 LD50) abamectin during organogenesis showing severe bilateral dilatation of renal pelvis (right) and a control one (left).

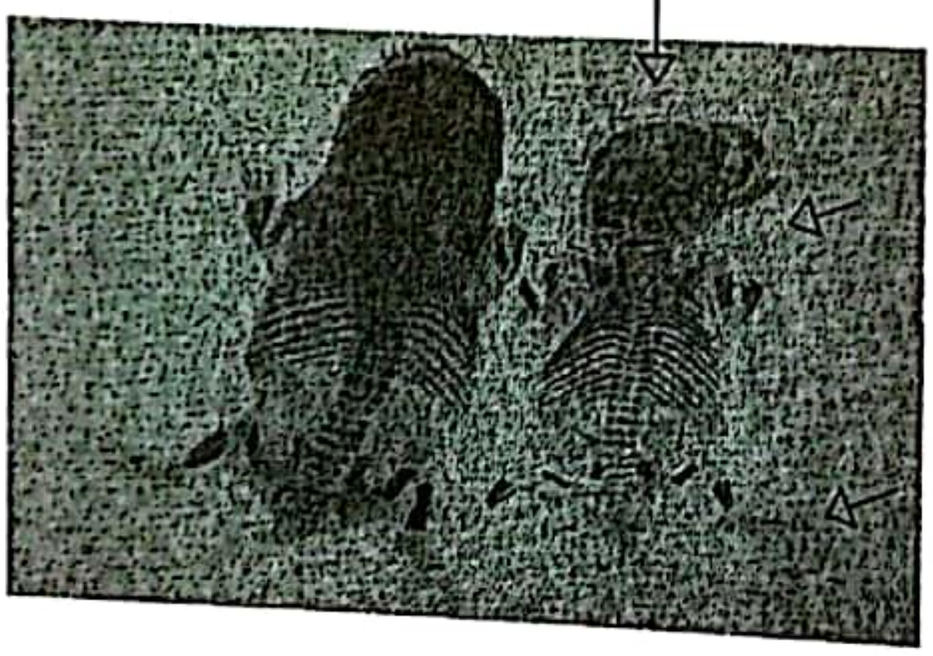

Fig. (8): A rat fetus obtained from a dam treated orally with 1.42 mg/kg bw (1/20 LD50) abamectin during organogenesis showing incomplete ossification of skull and absence of phalanges (right) and a control one (left)

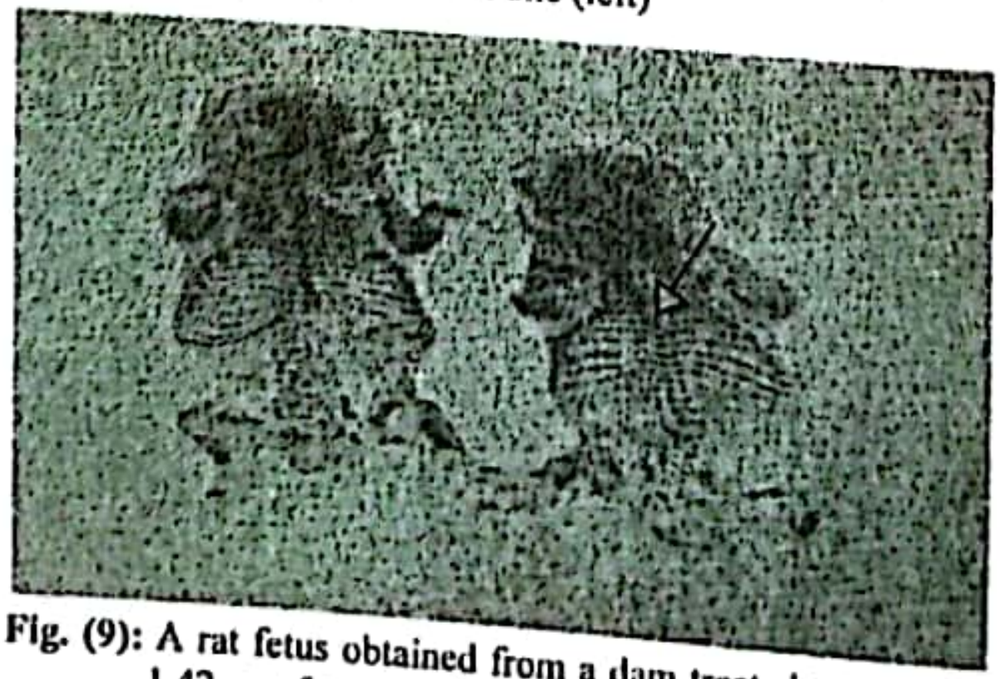

Fig. (9): A rat fetus obtained from a dam treated orally with 1.42 mg/kg bw (1/20 LD50) abamectin during organogenesis showing absence of sternebrae (right) and a control one (left).

Fig. (10): A rat fetus obtained from a dam treated orally with 1.42 mg/kg bw abamectin during organogenesis showing reduction in the number of sternbrae (right) and a control one (left).

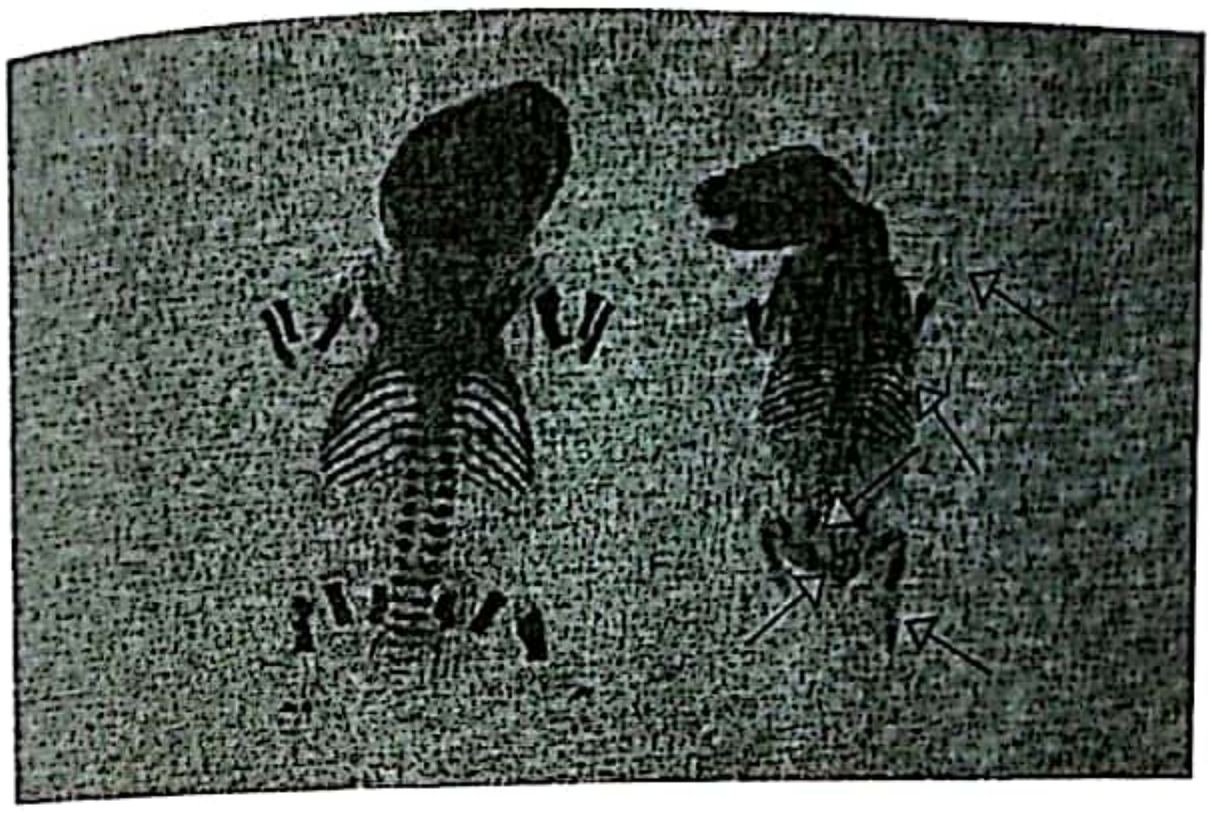

Fig.(11): A rat fetus obtained from a dam treated orally with 1.42 mg/kg bw abamectin during organogenesis showing wavy ribs, absence of phalanges, sacral and caudal vertebrae (right) and a control one (left)

Fig.(12): Section in placenta of a rat fetus obtained from a dam treated orally with 2.85 mg/kg bw abamectin during organogenesis showing cell necrosis with pyknotic nuclei (a) and desquamation of chorionic villi epithelia(b) (H&E. X20).

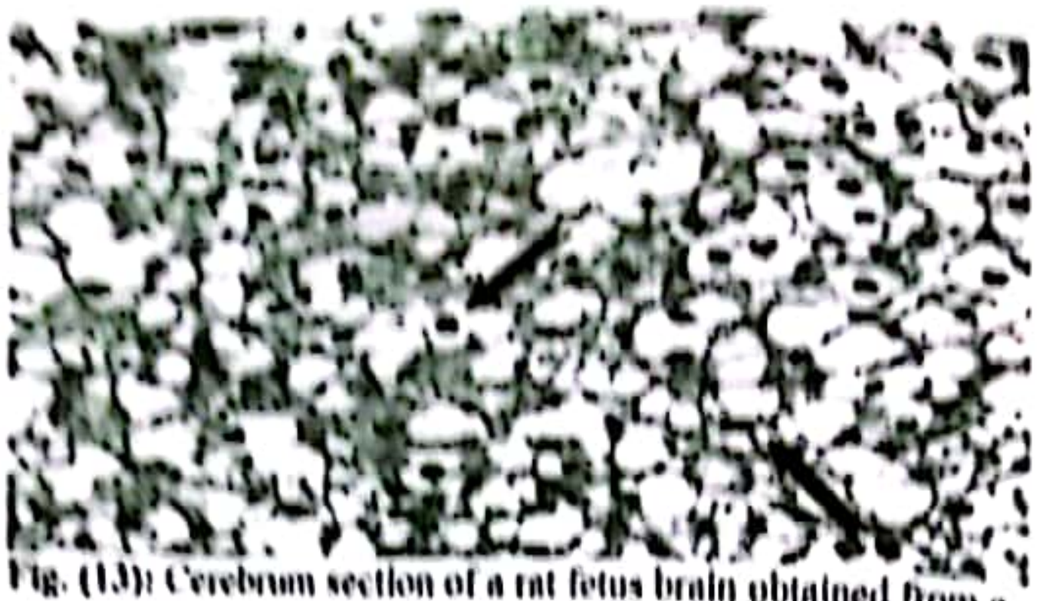

Fig. (13): Cerebrum section of a rat fetus brain obtained from a dam treated orally with 1.42 mg/kg bw abamectin during organogenesis showing cytoplasmic vacuolation and pyknotic nuclei of neuronal cells (H&E. X40).

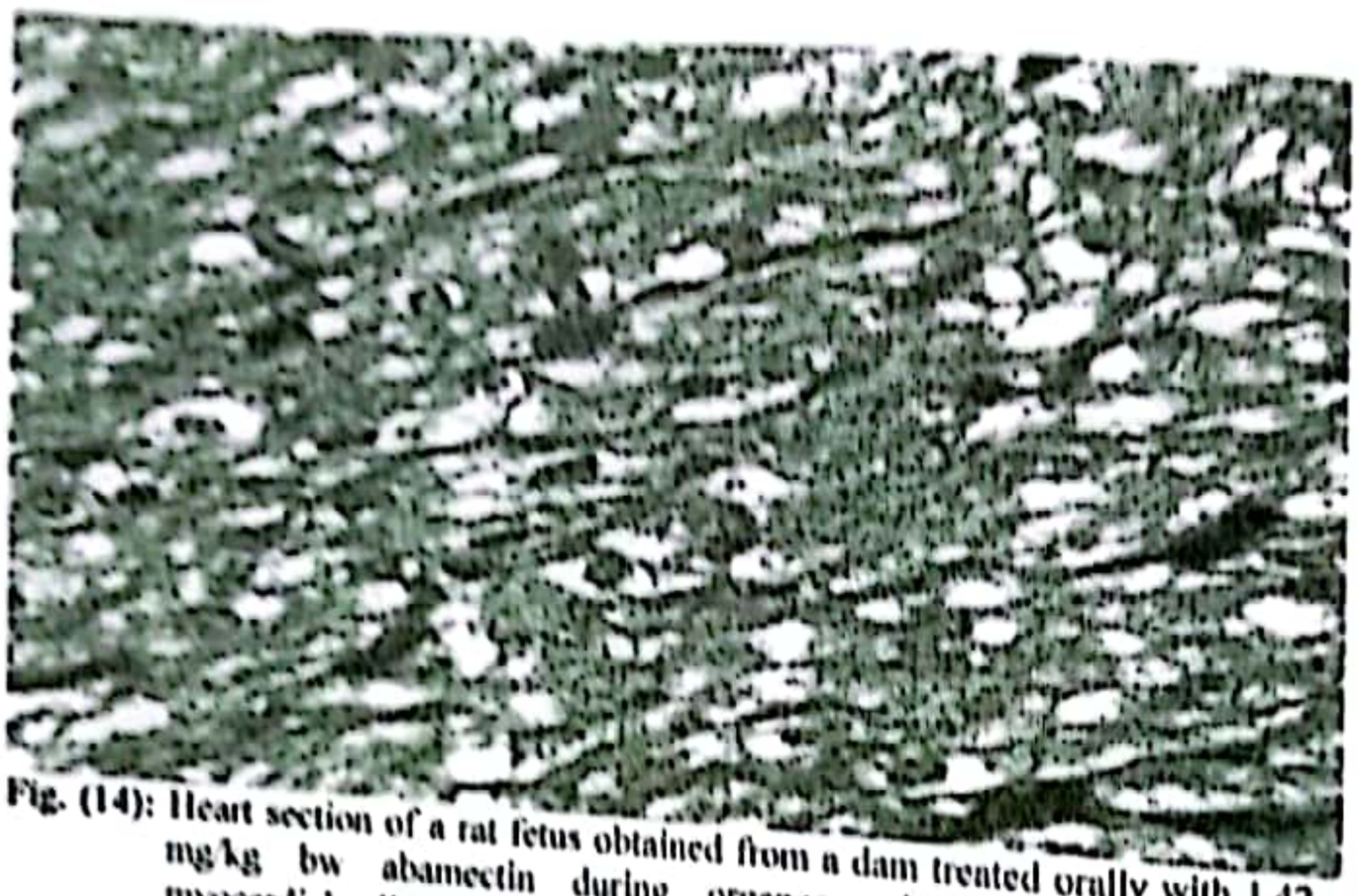

Fig. (14): Heart section of a rat fetus obtained from a dam treated orally with 1.42 mg/kg bw abamectin during organogenesis showing vacuolated myocardial cells and loss of longitudinal and cross striations, (H&E.).

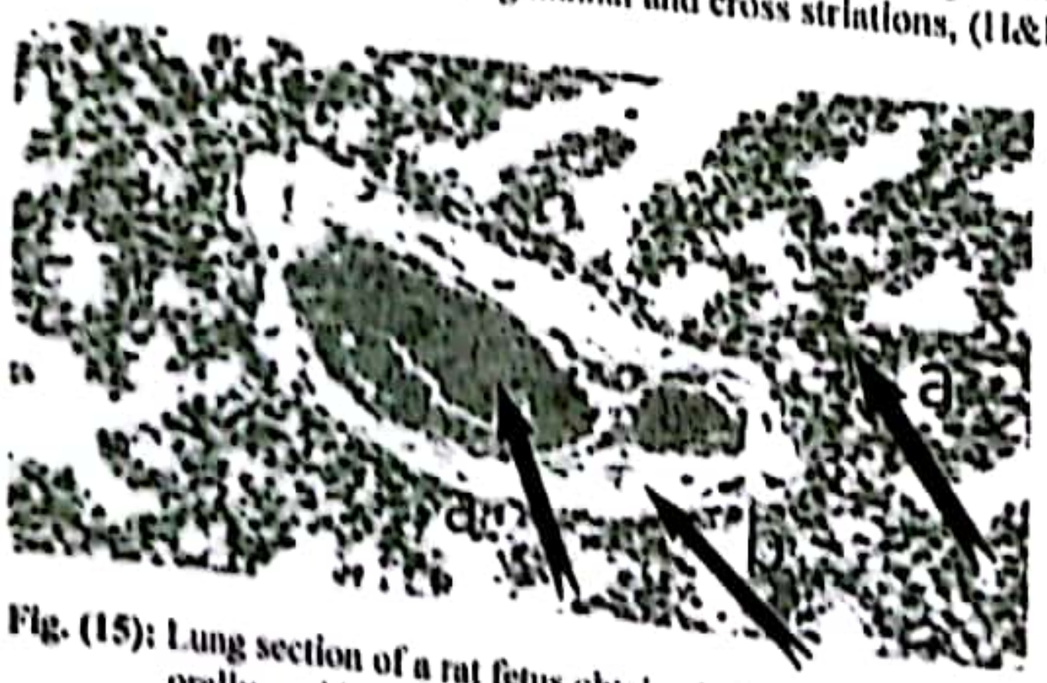

Fig. (15): Lung section of a rat fetus obtained from a dam treated orally with 2.85 mg/kg bw abamectin during organogenesis showing congestion of blood vessels and alveolar walls (a), perivascular edema (b), and vacuolation of alveolar lining epithelia (H&E. X20).

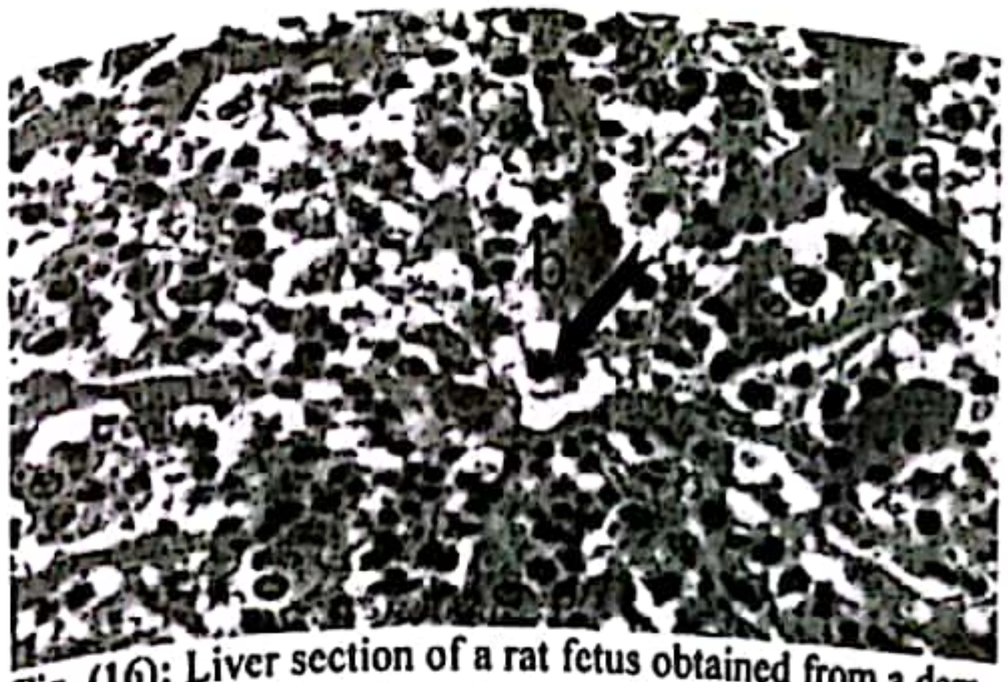

Fig. (16): Liver section of a rat fetus obtained from a dam treated orally with 2.85 mg/kg bw abamectin during organogenesis showing sinusoidal congestion (a), hydropic degeneration of hepatocytes (cell vacuolation with centrally located pyknotic nuclei and remain of cytoplasm)(b), (H&E. X40).

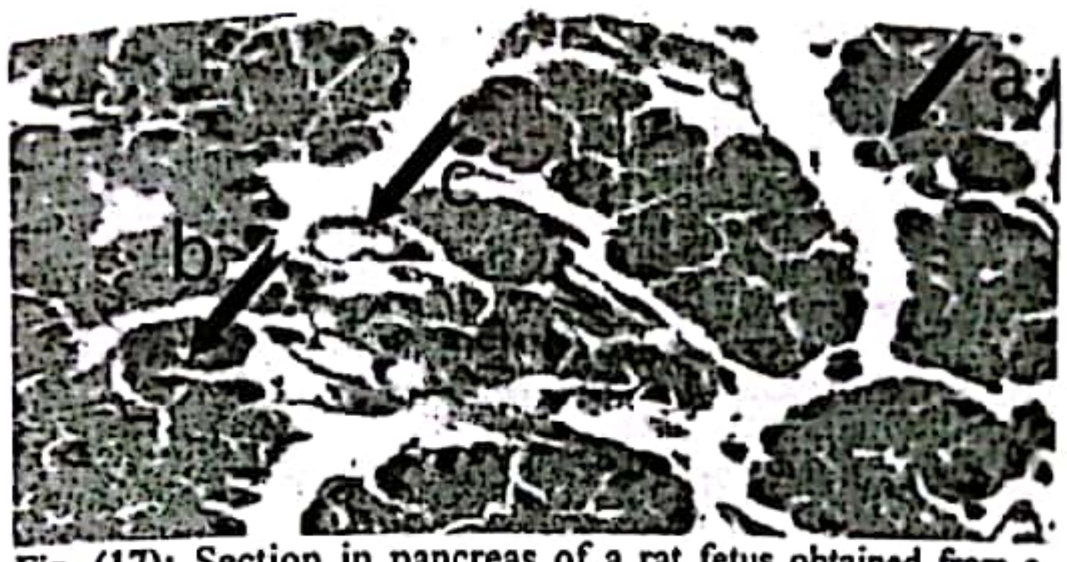

Fig. (17): Section in pancreas of a rat fetus obtained from a dam treated orally with 2.85 mg/kg bw abamectin during organogenesis showing loss of zymogen granules, pyknotic nuclei of pancreatic cells (a), and congestion of islets of langerhans (b) with reduction in their size due to cell necrosis (c), (H&E. X40).

Fig. (18): Kidney section of a rat fetus obtained from a dam treated orally with 2.85 mg/kg bw abamectin during organogenesis showing granular cytoplasm, pyknotic nuclei, vacuolation of tubular epithelia (a), cloudy swelling in tubular cells and complete destruction of some cells(b).The glomeruli are congested with hyper cellularity and narrowing of Bowman's space (c), (H&E. X40).

DISCUSSION

Abamectin is a widely used insecticide and acaricide in many parts of the world (U.S. EPA, 2004). It may have the potential to cause reproductive toxicity (Gordon et al., 1982a and U.S. EPA, 2008).

The oral LD_{50} of abamectin 1.8% EC was determined in this study as 28.5 mg/kg bw. Previous studies showed that the oral LD_{50} of abamectin in rats is 11 mg/kg (Lankas and Gordon, 1989). Merck Research Laboratories (1993) reported that the oral LD_{50} for the 1.8% w/v abamectin EC in rats was 300 mg/kg. Other studies determined its acute oral LD_{50} in rats in the range of 4.4 to 11.8 mg/kg in males and 10.9 to 14.9 mg/kg in females (U.S. EPA, 2004). These variations in the acute oral LD_{50} values may be due to the difference in the environmental condition, strain and genotype of animals which controls their sensitivity to abamectin toxicity.

The target organ of abamectin was the nervous system, symptoms of poisoning previously observed in laboratory animals included pupil dilation, salivation, vomiting, convulsions and/or tremors, and coma (European Food Safety Authority, 2008) and these signs of toxicity coincidence with those appeared on the exposed rats in our study. These signs could be attributed to the interaction of abamectin with gamma-aminobutyric acid receptor (Coccini et al., 1993).

In the present study there was no evidence of maternal toxicity at any of the tested dosage levels of abamectin along exposure period of the teratological investigation. Abamectin at all dosage levels caused no or insignificant elevation in the percentages of early or late resorption sites and insignificant reduction in the percentages of live fetuses compared with control groups. Hence, the ability of the dams to support implantation, placentation and early embryonic development was not different from that of dams in the control group as previously shown by Robertson (1977), Gordon et al. (1983) and Gordon et al. (1985) in treated mice.

There was reduction in average fetuses and placental weights that was dose related with the presence of dwarf fetuses especially on exposure to 2.85 mg/kg bw and 1.42 mg/kg bw. Also, the incidences of the visceral and skeletal malformations in the examined fetuses were significantly increased on exposure to the two high doses. Similarly, Gordon et al. (1982a) gave abamectin to rats at dosage levels of 0.4, 0.8 or 1.6 mg/kg bw/day on days 6 through 19 of gestation, and found an increased incidence of fetuses with external fetal malformations (exencephaly, cleft palate, gastroschisis), visceral malformations (higher incidence of distended ureters) and skeletal abnormalities (higher

incidence of fetuses with lumbar ribs and lumbar count variation) were recorded in the treated groups at all doses.

In rabbit, Gordon et al. (1982b) administered abamectin at oral dosage levels of 0.5, 1 or 2 mg/kg bw/day on day 6 through 27 of gestation to groups of female New Zealand albino rabbits. The results showed that fetuses of the 2 mg/kg bw/day had cleft palates, omphaloceles, clubbed forefeet, vertebral malformations, branched and fused ribs at higher incidences than in the control group with increased incidences of incompletely ossified sites particularly in sternebrae and metacarpals.

Our results disagree with Gordon et al. (1987b, 1988) who found no evidences of embryotyoxicity or teratogenicity in two oral developmental toxicity studies on female CF-1 mice after oral treatment with abamectin at dosage levels of 0.25, 0.5 and 1 mg/kg bw/day on days 6 through 15 of gestation.

The placenta plays a critical role in regulating the exchange of various substances as nutrients, hormones, and other molecules essential for the maintenance of pregnancy and normal fetal development between the maternal and fetal circulation throughout gestation. It also protects the developing fetus from potentially detrimental environmental xenobiotics. However, this barrier is incomplete as drugs and toxins can diffuse across the placenta (Syme et al., 2004). Multidrug resistance phosphoglycoprotein (Pgp) in placenta is responsible for preventing transplacental transfer of substrates from mother to fetus (Smit et al., 1999 and Schinkel and Jonker, 2003). The multidrug resistance phosphoglycoprotein is plasma membrane protein that functions as an ATP-dependant efflux pump, preventing entry of specific endogenous and exogenous wide range of structurally and functionally diverse xenobiotics as well as glucocorticoids into the fetal compartment (Cordon-Cardo et al., 1990 and Ambudkar et al., 2003).

Previously, an increase in the expression of genes encoding for Pgp (ABCB1) within fetal organs (including skin, kidney, intestines) with advancing gestation had been shown. This increase in fetal organ expression may provide compensation for the reduction in placental protection (Kalabis et al., 2005). Other fetal protective mechanisms, such as the cytochrome P450 enzyme system and phase 2 enzymatic pathways of xenobiotic metabolism are known to increase in late gestation, and they may provide additional compensatory fetal protection (Wells and Winn, 1996).

It has been reported that avermectins and other potential teratogens are Pgp substrate in human and animals (Didier and Loors, 1996; Scala et al., 1997 and Lankas et al., 1998).

The teratogenic and fetotoxic effects of abamectin mainly referred to placental multidrug resistance phosphoglycoprotein

(Pgp) deficiency and transplacental transfer of abamectin from mother to the fetus that was proved to be a substrate of placental Pgp (Lankas et al., 1998; Smit et al., 1999; Schinkel and Jonker 2003; Kalabis et al., 2005 and Petropoulos et al., 2007).

Therefore, the recorded teratogenic effects following abamectin exposure in our results could be attributed to transplacental transfer of abamectin from mother to the fetus that was proved to be a substrate of placental Pgp and/or to the direct cytotoxic effects of abamectin on placenta which was confirmed by the recorded placental histopathological changes. Also, it may be attributed to its mutagenic effect which had been proved in rat liver cell cultures (U.S. EPA, 1990). The observed histopathological alterations in the examined rat fetuses' internal organs as brain, lung, heart, liver and kidneys confirm the role of abamectin in the induction of these organs abnormalities. In summary, our results strongly suggest the teratogenic potential of abamectin following exposure of pregnant animals during the organogenesis period.

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التأثيرات المسخية للابامكتين فى الجيرزان

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تم دراسة الأثار المسخية لمبيد الأبامكتين عقب اعطاؤة لاناث فئران بيضاء حوامل بجرعات ٢,٨٥، ١,٤٢، ٠,٧٢ مجم / كيلوجرام من وزن الجسم (١/١٠ ، ١/٢٠، ١/٤٠من الجرعة المميتة لنصف عدد الحيوانات، على التوالى) خلال فترة تخليق الأعضاء. وجد أن العلاج بالأبامكتين لم يؤثر على الحالة التناسلية (عند أماكن الإنغراس و الامتصاصات الجنينية ، الأجنة الحية والميتة لكل ولدة) عند كل الجرعات. ولكنه تسبب فى إرتفاعَ معنوىَ في النِسَب المئويةِ مِنْ أجنةِ الفئران التى بها تشوهات مورفولوجيه، حشويه و عظميه عند التعرض للجرعتين الأعلى بالمقارنة بالمجموعة الضابطة. بالاضافة الى هذا، تسبب الأبامكتين فى حدوث تغيرات هستوباثولوجية بالمشيمة و بالأعضاء الداخلية للجنين بدرجات مختلفة تعتمد على الجرعة.