# Experimental study on lethality and toxicological effects of Naja haje, Naja nubiae and Cerastes cerastes crude venoms in rats

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## Abstract

**Background:** snake venoms are complex mixtures of enzymatic and non-enzymatic components with specific pathophysiological effects that differ widely between and within species

**Objective:** this study was designed to investigate the lethality and toxicological effects of snake venoms of Naja haje, Naja nubiae and Cerastes cerastes on experimental rats

**Methods:** lethality test was conducted in 3 groups of albino rats (5 each). Group 1: N.haje venom (0.2mg/kg, i.p.), group 2: N.nubiae venom (0.4mg/kg, i.p.), group 3: C.cerastes venom (0.5mg/kg, i.p.). Time of death for each group was recorded. $LD_{50}$ of N.haje snake venom was determined as it was found to be the most

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poisonous one among the three venoms. Behavioral and neurological effects of the venom were tested into 3 groups of rats (5 each). Group1: control (normal saline), group 2: N.haje venom (0.18mg/kg, i.p), group 3 N.haje venom (0.5mg/kg, i.p). To study fetotoxicity, pregnant rats were divided into 2 groups (5 each). Group 1: control group and group 2: N.haje venom toxic dose: 0.18mg/kg, i.p. Both groups were observed for the continuity of pregnancy and fetuses were examined for presence of any external abnormalities.

**Results**: N.haje snake venom was the most poisonous one among the three snake venoms as it has the lowest minimal lethal dose (0.2mg/kg) and quick death time (46 min ± 3). Minimal lethal doses and mean time of death of N.nubiae and C.cerastes were 0.4mg/kg, 0.5 mg/kg and 90min±15, 180min±20 min, respectively. $LD_{50}$ of N.haje venom was 0.28mg/kg. Convulsions and paralysis were most significant neurotoxic effects of N.haje venom. Toxic dose of N.haje venom (0.18mg/kg) didn't affect continuity of pregnancy or induced external malformations on fetuses.

**Conclusion**: it could be concluded that, N.haje snake venom is most poisonous compared to Naja nubiae andCerastes cerastes venoms. Both toxic and lethal doses of N.haje snake venom induced neurotoxicity, but it didn't induce fetotoxicity.

**Key words**: Lethality, rats, snake venoms, Naja haje, Naja nubiae andCerastes cerastes

**مستخلص البحث**

الخلفية: سم الثعبان هو خليط مركب من بروتينات إنزيمية و لا إنزيمية ذات وظائف فسيولوجية مرضية محددة التي تختلف بإختلاف نوع الحية و بين افراد النوع الواحد.

**الهدف:** يهدف هذا البحث إلى دراسة التأثيرات السمية لسموم الكوبرا المصرية، الكوبرا النوبية و الأفعى القرناء على جرذان التجارب.

**الطريقة:** في البدء تم إجراء اختبار لتحديد الأفعى الآكثر سمية و الأسرع فتكا وذلك بتقسيم مجموعة من جرذان التجارب الى ثلاث مجموعات، المجموعة الأولى حقنت بجرعة (0.2 مج/كجم) سم الكوبرا المصرية و الثانية حقنت بجرعة (0.4 مج/كجم) سم الكوبرا النوبية و المجموعة الثالثة حقنت بجرعة(0.5 مج/كجم ) من سم الأفعى القرناء. تم حساب الجرعة نصف القاتلة لسم لكوبرا المصرية كونها الاكثر سمية و الاسرع فتكا بين سموم الثلاث افاعي ؛ من ثم تم تقسيم مجموعة أخرى من جرذان التجارب الى ثلاث مجموعات(٥ جرذان لكل مجموعة)، حقنت المجموعة الأولى بمحلول فسيولوجي (كلوريد الصوديوم) و التي استخدمت كمجموعة ضابطة، المجموعة الثانية حقنت بجرعة سامة مقدارها(0.18 مج/كجم) من سم الأفعى المصرية، اما المجموعة الثالثة فقد حقنت بجرعة قاتلة (0.5 مج/كجم) من سم الكوبرا المصرية؛ على هذه المجموعات الثلاث تمت ملاحظة التغيرات العصبية و السلوكية. قسمت مجموعة من الجرذان في مرحلة الحمل المبكر الى مجموعتين؛ حقنت المجموعة الأولى بمحلول فسيولوجي (كلوريد الصوديوم) كمجموعة ضابطة، المجموعة الثانية حقنت بجرعة سامة مقدارها(0.18 مج/كجم) من سم الأفعى المصرية، وتمت الملاحظة اثناء فترة الحمل ومن ثم فحص الأجنة.

**النتائج:** وجدت الدراسة ان سم الكوبرا المصرية هو الأكثر سمية و الأسرع فتكا من بين الأفاعي الأخرى (الكوبرا النوبية و الأفعى القرناء) اذ يساوي الحدالأدنى من الجرعة المميتة لسم هذه الكوبرا (0.2 مج\كجم) مع متوسط زمن حدوث الوفاة مساو ل46±3 دقائق. بينما الحد الأدنى للجرعة المميتة و متوسط حدوث الوفاة للكوبرا النوبية و الأفعى القرناء هما (0.4 مج\كجم و 0.5 مج\كجم) و(90±15و 180±20دقيقة) على التوالى، الجرعة نصف القاتلة لسم الكوبرا المصرية هي(0.28 مج/كجم). ظهرت التأثيرات السمية العصبية لسم الكوبرا متمثلة في تشنجات و شلل في كلتا المجموعتين. ، ايضآ وجدت الدراسة أن الجرعة السامة من سم الكوبرا المصرية لم تتسبب في حدوث تشوهات خلقية للأجنة و كذلك لم تؤثر على استمرارية الحمل بشكل طبيعي.

**الخاتمة:** الكوبرا المصرية من اكثر الافاعي الخطرة في السودان؛ الجرعة المميتة و الجرعة السامة من سم الكوبرا المصرية ذاتا تأثيرات سمية عصبية و ليس لدى الجرعة السامة أي تأثيرات على الأجنة.

## INTRODUCTION

Envenoming and deaths resulting from snake bites has always been a global health issue as well as in Sudan, especially in rural areas and areas with inadequate medical services, this why this study was conducted [1].

Snake venoms are complex mixtures of 50 or more components that function to immobilize, kill, and pre-digest prey. In human victims these substances cause local digestive or cytotoxic effects on tissues as well as hemotoxic, neurotoxic, nephrotoxic and other systemic effects [2]. There is a large

degree of variability in venom constitutions at all taxonomic levels. Furthermore, within the same species the toxic components of the snake venom differ greatly among populations and across geographical areas [3]. Assessment of the toxicological effects of venomous snake's species in Sudan is a critical step for an efficient determination of the venom activity and increase the understanding of geographical intraspecific variation in venom composition and improving snake bite treatment by designing specific anti-venom.

Cerastes cerastes or the desert horned viper widely distributed in North Africa including Sudan. Envenomation by this species usually causes hemorrhage, necrosis, swelling, nausea, vomiting and hematuria [4]. Naja haje (Egyptian cobra) is a non-spitting cobra of elapid family. Envenomation causes severe swelling, local pain, necrosis, bruising, collapse or convulsions accompanied with moderate to severe flaccid paralysis [5]. Naja nubiae (the Nubian cobra) is a species of spitting cobra native to Africa. In sudan, Naja nubiae distributes in Nile valley and Darfur [6]. Symptoms of envenomation involve swelling at the bite site with blistering and bruising that may lead to necrosis [7].

The present study was conducted to measure the lethality of the venoms of N.haje, N.nubiae and Cerastes cerastes

snakes present in Sudan. According to the minimal lethal dose, time of death and severity of signs before death, the most poisonous snake venom was selected and subjected to further experimentation: determination of the $LD_{50}$, measurement of behavioral and neurological changes at two different doses of this venom and to test effect of its toxic dose on pregnant rats at early stage and on their fetuses.

# MATERIAL AND METHODS

## Experimental animals

Males and females Wistar albino rats weighing $180 \pm 30$ gm were used. Rats were obtained from Experimental Animal Unit; Faculty of Veterinary Medicine, University of Khartoum, then housed at animal room in faculty of pharmacy, International University of Africa. Animal room was under controlled conditions of temperature ($25$ cº) and relative humidity ($50\%$) as well as $12$ hours light/ dark cycle with light between $7$ am to $7$ pm. Rats were allowed free access to food (standard rodents chow) and water ad libitum.

**Snakes:**

The following types of snakes were used:

Naja nubiae (family Elapidae), Naja haje (family Elapidae) and Cerastes cerastes (family Viperidae)

These snakes were obtained from Sudan natural history museum (Khartoum, Sudan). These snakes were collected from different regions of Sudan by a professional hunter. Each snake was housed individually under standard conditions and fed on frogs, chicks and lizards.

## METHODS

### 1. Venom collection and preparation:

Fangs of snake were put on container covered by plaster then venom was milked by massaging the gland below the eye in dim light. Collected venom was lyophilized using thermo freeze dryer, then stored in light resistant container at 4ºC and reconstituted in saline solution prior to use.

### 2. Preparation of venom working solution:

10 mg of snake venom was weighed and dissolved in 1 ml normal saline (stock venom solution). Working venom / saline solution of 1mg/ml was prepared by 1: 10 dilution.

### 3. Selection of minimal lethal and toxic (non-lethal) venom doses:

To determine the minimal lethal dose of each one of the three venoms, different doses were tried in groups of animals (5 rats each), starting with 1mg/kg then decreased stepwise and least venom dose that caused death within 24 hours was considered minimal lethal venom dose. Half of this minimal lethal dose was

considered maximum toxic (sub-lethal) dose. These trials were conducted for venoms of the three snakes (Naja haje, Naja nubiae and Cerastes cerastes).

**4. Determination of $LD_{50}$ of N.haje snake venom:**

Median lethal dose ($LD_{50}$) was calculated using karber method [8]. Thirty rats were divided into 6 groups (5 rats each). A series of doses ranging between $LD_{100}$ (0.5mg/kg) and $LD_0$ (0.05mg/kg) were determined. These doses were: 0.25, 0.18, 0.12 and 0.0625mg/kg. Each group received a specific dose. Number of dead rats in each group was recorded during 24 hours post injection and $LD_{50}$ was calculated using this equation:

$LD_{50} = LD_{100} - \sum (A*B)/N$

Where:

A = the difference between two successive doses of administered venom

B = the average number of dead rats in two successive doses

N = total number of rats in a group

**5. Measurement of neurological and behavioral changes:**

Envenomed rat groups were observed for neurological and behavioral toxicity. For recording of behavioral toxic effects, structured observation sheet at time intervals: 15, 30 and 60 min. following scoring system is adopted:

0 = no change, + = slight increase, ++ = moderate increase, +++ = high increase, − = slight decrease, − − = moderate decrease, − − − = high decrease in response compared to normal behavior

**6. Assessment of fetotoxicity:**

Method described by AL-Harbi et al [9] and ElTahir et al [10] were used. Adult female Wistar albino rats were allowed to mate with proven male rats in a ratio of 1 male to 1 female. Presence of vaginal sperm was taken as an indicator of copulation and that day was considered as day one of pregnancy. Toxic dose (0.18 mg/kg) of N.haje venom was injected on day 7 of pregnancy ($GD_7$) and observed for continuity of pregnancy. Delivery of fetuses was allowed to be by spontaneous parturition. Number of live and dead fetuses was recorded; live fetuses were weighed individually and each fetus was examined for any external abnormalities.

**Experimental design:**

**1. Design to determine minimal lethal dose of each snake venom:**

Initially, rats were divided in 3 groups (5 rats each):

Group 1: 1mg/kg, i.p., Naja haje venom

Group 2: 1mg/kg, i.p., Naja nubiae venom

Group 3: 1mg/kg, i.p., Cerastes cerastes venom

According to finding of these doses, consecutive doses for each venom were used and finally the minimal lethal doses were determined. These groups were observed for lethality during 24 hours. Times of deaths were recorded. Snake venom with lower lethal dose and shorter time of death, was considered the most poisonous venom among the three.

**2. $LD_{50}$ study design:**

To determine $LD_{50}$ of N.haje snake venom, which was found to be most poisonous one, rats were divided into 6 groups (5 rats each):

Group 1: received 0.5 mg/kg ($LD_{100}$)

Group 2: injected with 0.25 mg/kg

Group 3: envenomed by 0.18 mg/kg

Group 4: received 0.12 mg/kg

Group 5: injected with 0.0625 mg/kg

Group 6: received 0.05 mg/kg ($LD_0$)

**3. Behavioral and neurological toxicity study design:**

For measurement of behavioral and neurological toxicies of N.haje venom, rats were divided in 3 groups (5 rats each) as follows:

Group 1: control group (0.9% Na Cl, i.p.)

Group 2: toxic non-lethal dose (0.18mg/kg, i.p.) of N.haje venom

Group 3: maximal lethal dose (0.5mg/kg, i.p.) of N.haje venom

**4. Fetotoxicity study design:**

Pregnant female rats were divided in 2 groups (5 rats each):

Group 1: control group (0.9% Na Cl, i.p.)

Group 2: toxic non-lethal dose (0.18mg/kg, i.p.) N.haje venom

**Statistical analysis:**

Date were statistically analyzed using SPSS software version 24 and presented as mean and standard error (SEM). Parameters of envenomed groups were compared to control group using one-way analysis of variance (ANOVA). Results were considered significant at $P < 0.05$.

**Ethical consideration:**

Permission of this experimental study had been obtained from International University of Africa – department of pharmacology

## RESULTS AND DISCUSSION

**1. Lethality of Naja haje , Naja nubiae and Cerastes cerastes snake venoms**

Generally, lethality of snake venom depends on a combination of its potency, volume of venom injected into the prey and the size of the victim. In the present study, Table1 shows the minimal lethal dose and time taken for death following envenomation with different snakes (**Naja haje, Naja**

**nubiae** and **Cerastes cerastes**) considered as an indicators of the lethality of the venom.

Naja haje venom appeared to be the most poisonous one among the 3 snakes as it has the least minimal lethal dose (0.2mg/kg) with mean time of death for rats received this venom 46 ± 3 min, Naja nubiae in the second place with minimal lethal dose equal to 0.4mg/kg and mean time of death 90 ± 15 min, venom of Cerastes cerastes appeared to have the highest minimal lethal dose (0.5mg/kg) with mean time of death 180 ± 20 min.

These findings are supported by the facts that Cerastes cerastes (the horned viper snake) of family Viperidae which is more hemotoxic than other families of snakes. Viper venom contains several components which promote or inhibit hemostatic mechanisms including coagulation, platelet function, fibrinolysis and vascular integrity [11]. Moreover, the bio distribution of viper venom from the site of injection to its numerous targets is supposably slow and partial, consistent with the fact that molecules in viper venom are medium and high molecular weight (20 – 60 KDa) compound that could have a longer residence time at the site of inoculation thereby reducing the venom bioavailability [12].

On the other hand, Naja haje and Naja nubiae (Cobras) are of Elapidae family they are mainly neurotoxic. Neurotoxic venom tends to act more quickly [13] by affecting the nervous system, stopping transmission of nerve signals to muscles, heart and lungs causing death due to complete respiratory failure [7].

Cobra venom consist of small size molecules (MWT<15 KDa), such small molecules could have a shorter residence time at the site of injection causing an instant and complete bioavailability in the blood [12].

In the current study, the Egyptian cobra venom (N.haje) was found to have rapid lethality than the Nubian cobra venom. N.haje snake is a non-spitting cobra and its venom is mainly neurotoxic (act more quickly), whereas Naja nubiae is a spitting cobra that's have the ability to spit or spray venom from their fangs into the eyes or skin of the victim, spitting cobras are characterized by cytotoxic pattern of envenomation [14]. The abundance of cytotoxic $PLA_2$ and cytotoxins in the venom of N.nubiae is proposed to be the main factor for its clinical features of cytotoxicity. Kazandjan et al.[15] stated that, most spitting cobra venoms are remarkably cytotoxic a part from the neurotoxic and cardiotoxic effects typical of other cobra species. So our findings are consistent with the general consideration that spitting cobras are primarily cytotoxic with little, if any

neurotoxicity [16, 17]. Furthermore, the rank of world atlas classified venom of N.nubiae to be less toxic than N.haje venom which supported results of this study.

**2. $LD_{50}$ value Naja haje snake venom**

The estimation of snake venom median lethal dose ($LD_{50}$) is an essential step for an accurate evaluation of the toxic activity of specific venom and is also frequently used to select the relevant anti-venom batch in addition to establish the neutralizing capacity of each vial, according to WHO, venom lethality is expressed as median lethal dose ($LD_{50}$) [18] .

In this study, $LD_{50}$ of N. **haje** venom was determined via intraperitoneal injection of the venom in rats by Karber method (Table 2), according to this method the approximate $LD_{50}$ for N.haje snake venom was determined to be equal to 0.28 mg/kg. In the study of Robert et al. [19] the subcutaneous $LD_{50}$ of N. **haje** venom in mice was reported to be 1.75 mg/kg. Other finding obtained by Ghazala et al. [18] demonstrated that, the intravenous $LD_{50}$ of the crude venom of N. **haje** venom in rats was found to be 0.28 mg/kg, whereas $LD_{50}$ equal to 0.25 mg/kg of N.haje venom by intramuscular injection into rats was found by Saeed et al. [20] .

$LD_{50}$ methods have many intrinsic variables and factors that affect the toxicity results; one of these factors is the route of

administration. Lethality of the venom varies with change in the route of administration; generally the $LD_{50}$ values obtained in animals injected intravenously were lower than those acquired by intraperitoneal and intramuscular injection [12, 18] .

Lethality of snake venom differs from species to species and even among individuals of the same species and this referred to multiple factors such as geographical location; most of the venom obtained from the same species with different geographical location has different $LD_{50}$ values [18]. Furthermore, seasonality, age of snake, genetic variations, and health of the snakes could potentially affect the $LD_{50}$ values of the venom. The typical species of the targeted animals, its body weight and health also considered influencer variables which impact the lethality of the venom and the values of the $LD_{50}$. In the study performed by R.M Douglas [21] to investigate the response of different animals to the same snake venom he found that, sheep's and horses are more susceptible to elapid venom than the other animals in the experiments ( mice, guniea pigs and monkeys ) and stated that different animals have different reactions to the same snake venom.

### 3. Behavioral changes induced by Naja haje venom

In the present study, both envenomed groups with two different doses of N.haje venom (toxic and lethal) showed

decrease in motor activity at 15 and 30 minute time intervals (Table 3). This is referred to the action of snake neurotoxins which mainly intent the neuromuscular junction of skeletal muscle where the motor nerve terminal and the nicotinic acetylcholine receptors at the motor endplate are the dominant target sites [22]. Behavioral manifestations after snake bites have been mentioned in several case histories each involving varying degrees of motor weakness [23].

Comparing findings from different studies is difficult as there is a lack in the published experimental works studied the effect of N.haje venom on the motor activity of rats.

**4. Neurological effects induced by Naja haje venom**

Neurotoxicity is a common feature of envenomation by elapids such as Naja species. Acute neuromuscular paralysis is the principal type of neurotoxicity and it's an important cause of mortality and morbidity related snake bite.

In the current study, group of rats that received the lethal dose of the venom (0.5 mg/kg), showed convulsions then peripheral paralysis within 15 min of envenomation, whereas the group that treated by the toxic dose (0.18 mg/kg), exhibited convulsion and peripheral paralysis after 30 min of the envenomation (Table 4). The neurotoxic effects of the Egyptian cobra are referred to the presence of highly potent á neurotoxins

which are post synaptic neurotoxins that bind and antagonize the nicotinic acetylcholine receptor at the neuromuscular junction resulting in systemic paralysis, respiratory failure and death [24,1]. In similar context Esmat et al. [25] illustrated that N.haje venom is highly lethal due to its content of alpha neurotoxin that's kill by paralyzing respiratory muscles in few minutes. Convulsions are one of the known preparalytic symptoms and signs after envenomation.

Campbell [26] revealed that, the onset of paralysis after envenomation with cobra venom has been shorter than its onset of bites from other snakes such as Australian and new quinea elapid.

**5. Effect of Naja haje venom on rat fetus**

As shown on table 5, maternal weight at day 1 of pregnancy is $220 \pm 10.5$ for the control group and $220.5 \pm 17$ for the envenomated group. The number of fetuses born for each group is $0.5 \pm 0.0$, the mean of fetal weight is $4.2 \pm 0.3$ for group 1 and $4.3 \pm 0.1$ for group 2. Fetal death is zero in both groups in addition to absence of gross abnormalities. Statistical analysis shows no significant difference in the maternal weight at day 1 of pregnancy between group 1 and group 2 ($P > 0.05$) and no significant change in the fetal weight ($P > 0.05$).

During pregnancy snake bites could be a risk to gestation maintenance which depend on the pregnancy period, maternal envenomation degree a long with the time of the beginning of envenomation [27,28,29] . Although snake bite envenomation during pregnancy not being entirely elucidated, the exposure to that venom during this period could lead to fetal growth retardant, teratogenic effect and mutation [29]

The present results showed that N.haje venom administered at toxic dose (0.18 mg/kg) on $GD_7$ didn't induce abortion or external anomalies (table 5). The fetuses appeared with normal skull form, ears, eyes, mouth and tail, foot conforming and anal drilling when compared with the control group. Furthermore, there was non significant change in fetal weight between the two groups.

To my knowledge and after extensive searching and reading, experimental records about the effect of N.haje snake venom on the continuity of pregnancy and induction of external malformations of fetuses weren't found in literature.

Study of Maria et al.[30] to investigate the effect of Bthrops jaraka snake venom on pregnant mice on $GD_5$, reported that, experimental groups revealed presence of external malformation, yet, it occurs in just one fetus what couldn't be

related to venom exposure. It remains uncertain whether snake venom crosses the placenta, although indirect evidence of placental transfer has been already represented in cases where adverse fetal effects occurred in the absence of adverse maternal effects [31,32,33]

## CONCLUSION:

In conclusion, the findings of this study revealed that, the venom of N.haje snake is one of the most poisonous venom found in Sudan with $LD_{50}$ equal to 0.28 mg/kg, both toxic and lethal doses of this venom induced neurotoxicity and the toxic dose didn't produce fetotoxicity.

**Table1. Lethality test Naja haje , Naja nubiae and Cerastes cerastes snakes venom**

| Name of snake | Dose (mg/kg) | Time of death (Mean± SEM) |
|---|---|---|
| Naja haje | 0.2 | 46 ± 3 min |
| Naja nubiae | 0.4 | 90 ± 15 min |
| Cerastes cerastes | 0.5 | 180 ± 20 min |

| Group | No of rats | Dose (mg/kg) | No of dead animals | Mortality % | Mean of death in 2 doses ( B ) | Dose difference ( A ) | (A*B) |
|---|---|---|---|---|---|---|---|
| 1 | 5 | 0.5 | 5 | 100 | – | – | |
| 2 | 5 | 0.25 | 2 | 40 | 3.5 | 0.25 | 0.875 |
| 3 | 5 | 0.18 | 1 | 20 | 1.5 | 0.07 | 0.105 |
| 4 | 5 | 0.125 | 1 | 20 | 1 | 0.055 | 0.055 |
| 5 | 5 | 0.0625 | 0 | 0 | 0.5 | 0.0625 | 0.031 |
| 6 | 5 | 0.05 | 0 | 0 | 0 | 0.0125 | 0 |
| | | | | | | | $\sum$ 1.06 |

**Table2. Median lethal dose ($LD_{50}$) of N.haje venom**

$LD_{50} = LD_{100} - \sum (A*B) / N$

$LD_{50} = 5 - 1.06/ 5$, $LD_{50} = 0.287$ mg/kg

**Table3: Behavioral effects of N.haje venom**

| Group number | Treatment groups | Dose (mg/kg) | Motor activity at different time intervals | | |
|---|---|---|---|---|---|
| | | | 15 min | 30 min | 60min |
| G1 | Control (normal saline) | 10ml/kg | **0** | **0** | **0** |
| G2 | Toxic dose of **N.haje** venom | 0.18mg | − | − | **0** |
| G3 | Lethal dose of **N.haje** venom | 0.5mg/kg | − | − | **Died** |

**−: decrease in motor activity, 0: normal motor activity**

**Table4. Neurological effects induced by Naja haje venom**

| Group number | Treatment groups | Dose (mg/kg) | Convulsions | Paralysis |
|---|---|---|---|---|
| G1 | Control (normal saline) | 10ml/kg | − | − |
| G2 | Toxic dose of **N.haje** venom | 0.18mg | + | + |
| G3 | Lethal dose of N.haje venom | 0.5mg/kg | + | + |

**+ = Present, − = Absent**

| Group No | Treatment/ Dose | Maternal Weight at day 1 of pregnancy | No of Fetuses Born | Fetal Weight(g) | Fetal death | Gross Abnormalities |
|---|---|---|---|---|---|---|
| G1 | Control (normal saline 10ml/kg | 220 ± 10.5 | 5 | 4.2 ± 0.3 | 0 | 0 |
| G2 | N.h venom 0.18 mg/kg | 220.5 ± 17 | 5 | 4.3 ± 0.1 | 0 | 0 |
| P value | | >0.05 | | >0.05 | | |

**Table5. Effect of Naja haje venom on rat fetus**

G1 statistically compared with G2, P > 0.05 considered statistically not significant

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