Peganum harmala extract antagonize counteracts the lethal effect of viper snake *Echis carinatus* venom in mice

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Abstract

This study evaluated possible antagonistic effects of *Peganum harmala* against the lethal effect of *E. carinatus* venom. Seventy-two albino mice were divided into 12 equal groups in 6 experimental protocols. The intraperitoneal was route of injection. In protocol **I,** Group A (control) treated with venom at 10 mg/kg. They died after 80 min averagely. In protocol **II**, Groups B_1 and B_2 were treated with 15 and 30 mg/kg of *P. harmala*, respectively and 10 mg/kg venom simultaneously. Their survival time increased to 232 and 210 min respectively. In protocol **III**, groups C_1 and C_2 were treated with 10 mg/kg venom and after 15 min received *P. harmala* at 15 and 30 mg/kg respectively. Their time to death was increased to 246 and 220 min respectively.

In protocol **IV**, groups D_1 and D_2, treated with pre-incubated of venom with *P. harmala* (30 min) at the previous doses. Their survival time increased to 211 and 195 min respectively. In protocol **V** groups E1 and E2 received only *P. harmala* extract (IP) at 15 and 30 mg/kg respectively. In protocol **VI**, groups F1, F2, and F3 received only *P. harmala* extract (orally) at doses of 15, 30, and 60 mg/kg respectively, they remained alive. *Peganum harmala* significantly ($p<0.05$) increased animal survival time thus, has an antagonistic effect against lethality effect of *Echis carinatus* venom, make it a possible antivenom candidate for further investigation.

Keywords: Snakebite, *Echis carinatus*, Venom, *Peganum harmala*, Antagonist, Mice

Introduction

Snakebites are a considerable global public health concern that pose a significant threat to both humans and animals. Approximately 5.4 million individuals being bitten by snakes annually, resulting in up to 138,000 fatalities.

Therefore, it is essential to promptly identify and provide appropriate treatment to minimize potential complications arising from envenomation [1,2].

Iran, located in West Asia, possesses remarkable biodiversity and a land of 81 snake species, 25 of which are venomous and hold significant medical concern importance. Among the venomous snakes found in Iran, the *E. carinatus*, (Figure 1) belongs to the Viperidae family, and predominantly found is in the southern of Iran [3]. *E. carinatus* is infamous for its aggressive behavior and a highly toxic venom, which primarily disrupts blood coagulation and the haemostatic system [4]. Research conducted by Warrell et al. (1977) has revealed that *E. carinatus* bites result in a higher mortality rate compared to other snake species found in Northern Africa and Asia [5]. From 2002 to 2011, Iran experienced 53,787 cases of reported snakebite incidents, and 67 deaths [6].

Antivenom (antivenin) is important mainstay and life-saving medication used to treat venomous bites and stings. It possesses the remarkable ability to neutralize venom toxins and alleviate their adverse effects. However, antivenom does have some disadvantages. Firstly, limited effectiveness as they may not be effective against all species or strains of venom. Additionally, there is a risk of allergic reactions in recipients, ranging from mild skin rashes to severe anaphylaxis, which can occur immediately following administration and pose a potential threat to life. Furthermore, antivenoms may not always be readily available, especially in remote areas or low-resource countries, because production of them can be expensive, making them less accessible to those who cannot afford them. Administering antivenoms can be complex, as they often require careful dosing and monitoring. In some cases, multiple vials may be needed, increasing the cost and logistical process. Moreover, their effectiveness in addressing localized tissue damage induced by venoms is limited and in severe cases local effects may lead to disability, permanent tissue loss, or amputation [7,8,9].

As a result, the development of improved treatments for envenoming is essential. to save more lives, with lesser complications. Therefore, scientists are searching for safer alternative treatment options that are easier to produce, store, transport, purchase, and administer, in order to overcome these barriers. In regions where snakebite incidents are prevalent and access to medical facilities is limited, plant-based medicine stands as an exceptional reservoir for seeking antivenom. In such regions, herbal remedies may represent the solitary opportunity to rescue the frail existence of sufferers [10,11]. In Bangladesh, only 10% of snake bite patients choose hospital treatment, while the majority relying on herbal remedies [12].

Medicinal plants consist of a variety of active phytochemicals, which display strong effectiveness against snake venom. Many herbal remedies are readily available as they grow in local environments and are easily affordable compared to synthetic medications. These remedies are believed to have fewer side effects due to their natural origins. However, It is worth noting that while herbal medicines have their advantages, the efficacy of many of them in traditional medicine as active agents against various effects induced by snakebite have not been scientifically investigated, nor have their active components been identified and isolated [13]. For instance, in tribal areas of India, rely on plant extracts to treat the severe local effects caused by the venomous viper snake *Daboia russelli russelli*, without any scientific validation [14]. In traditional Ayurvedic medicine Indian *Rauvolfia serpentine* is utilize to treat snakebite complications. *Andrographis paniculata*, also known as the "King of Bitters," has a long history in traditional medicine for its effectiveness in treating snakebites and venomous envenomation [10].

Certain traditional medicines with natural PLA2 inhibitors have strong anti-snake venom properties. For instance, the ashwagandha plant neutralizes speckled cobra venom [15], and the leaf extract of Acalypha indica neutralizes *russell's*

viper venom [11]. aqueous root extract of *Mimosa pudica* inhibited the hyaluronidase and protease activities of Indian snake (*Naja naja, Vipera russelli* and *E. carinatus*) venoms by in dose dependent manner [16]. These compounds interact with the active site of PLA2s, proving their efficacy as anti-inflammatory and antidotes [17].

It has been reported that *Tabernaemontana alternifolia* root extracts neutralize enzyme activities of *E. Carinatus* and *Naja naja* venom [18]. The compounds such as flavonoids, polyphenols, tannins, sterols, terpenoids, and polysaccharides, found in plants, neutralize the venom's hydrolytic enzymes, specifically phospholipases, proteases, and hyaluronidase. These compounds effectively combat the harmful impacts of the venom [13, 19]. They attach to the active sites of these enzymes or alter key residues that are significant for the enzymes' catalytic activity. As a result, the release of inflammatory, vasodilatory, and vasoconstrictive mediators that typically occur during envenomation is prevented. This, in turn, minimizes damage to local tissue, inflammation, myonecrosis, impairment of vital organs, and modifications in coagulation components [13, 20]. Furthermore, the curative efficacy of these botanical species in snakebite treatment could potentially stem from their intrinsic medicinal properties encompassing antioxidative, anti-inflammatory, anti-edema, antimicrobial, antipyretic, and wound-healing effects qualities.

Peganum harmala L, (Syrian Rue) is a perennial plant belonging to the family Zygophyllaceae [21,22]. It has been scattered from central Asia to the various regions of the world including Australia, North Africa, and southwestern America [22].

Peganum harmala, particularly in its seed, contains a variety of phytoconstituents mostly bioactive alkaloids [23], including harmine, harmalol, harmaline, harmol, vasicine, vasicinone, deoxyvasicine, deoxyvasicinone, and beta-carboline being

particularly significant [24,25]. Because of this, *P. harmala* exhibit numerous therapeutic benefits such as, Traditionally, it has been utilized in the treatment of various diseases such as diabetes, asthma, arthritis, hypertension, and others, across different cultural backgrounds. Also, it exhibits anticancer, antimicrobial, anti-inflammatory, antiviral, antidiarrheal, antiemetic, antidepressant, anthelmintic, and antioxidant therapeutic properties [26]. In Iran, the traditional practice of burning *P. harmala* seeds and utilizing the resulting smoke as a disinfectant is widely known.

There been unverified reports suggesting the use of *P. harmala* in certain regions of Iran for relieving bites and stings from various animal sources. However, it is important to note that these claims are not supported by scientific evidence or research. This study, therefore, aimed to investigate the potential of *P. harmala* as a treatment for snakebites, marking the first examination of its effectiveness against the lethal effects of *E. carinatus* snake venom.

Materials and Methods

Venom

The freeze-dried crude venom of *E. carinatus* was kindly provided by the Razi Vaccine and Serum Research Institute, in Karaj, Iran. It was stored at 4ºC and freshly prepared by dissolving it in a sterile saline solution to a final volume of 500 µl prior to injection into the animals.

Preparation of *Peganum harmala* extract

The *Peganum harmala* was harvested from agricultural fields near the city of Sabzevar (36°12′45″N and 57°40′35″E) in the western region of the Razavi Khorasan province in Iran and was identified at the Ferdowsi University of Mashhad Herbarium (13613-FUMH). After drying the plant material for two

weeks in a dark room at 28±4 °C, the black seeds separated and ground into a fine powder. The ethanolic extraction extract of *P. harmala* was then prepared at the Department of Pharmacognosy in the Pharmacy College of Ferdowsi University of Mashhad. About 100 grams of the powder were poured into a 500 ml Erlenmeyer flask, and 300 ml of methanol was added to the flask, covered approximately 2 cm above the surface of the powder. The resulting solution was stirred, covered, and stored in a dark location for 48 hours. Then the upper portion of the solution was filtered using Whatman filter paper no. 1. Methanol was added to the sediment portion and stirred for 30 minutes, and this process was repeated multiple times until the upper phase of the solution turned completely colorless. The resulting solution was subjected to a vacuum rotary evaporator (IKARV 10, Germany) set at 45 °C and 60 rpm. The solvent was gradually evaporated, eventually yielding a viscous extract. The extract was then transferred onto a plate and placed in an oven to fully eliminate the solvent. Finally, it was covered with aluminum foil and stored in a refrigerator at 4°C until use. Experiments were carried out utilizing different solutions and techniques to dissolve the extract, however, none yielded favorable results. Ultimately, it was found that the addition of 2 Normal HCL and pH adjustment to 7.5 with NaOH effectively dissolved the extract.

Animals

A total of 72 adult albino mice, 8-10 weeks and weighing 35±5 grams, were obtained from the Animal House at Mashhad University of Medical Sciences. The mice were housed in the animal facility at the Faculty of Veterinary Medicine, with controlled environmental conditions including a 12:12 light-dark cycle, a temperature of 22±3ºC, and a relative humidity of 55±10%. They were kept in standard rodent cages and provided with unlimited access to food and water. The

experimental protocol followed the guidelines of the Animal Ethics Committee at the Ferdowsi University of Mashhad (code: IR.UM.REC.1401.171).

Experimental protocols

The study performed through six different protocols (I-VI) (Table 1). A total of 72 mice were divided into 12 equal groups (A, B1, B2, C1, C2, D1, D2, E1, E2, F1, F2 and F3).

In protocol **I** (control), group A received only venom at a dose of 10 mg/kg, while In protocol **II**, groups B1 and B2 were simultaneously treated with 15 and 30 mg/kg of *Peganum Hermala* extract respectively along with 10 mg/kg of venom. In protocol **III**, group C1 and C2 were treated with 15 and 30 mg/kg of *Peganum Hermala* extract respectively, 20 minutes after receiving venom at 10 mg/kg. In protocol **IV**, group D1 and D2 received a mixture of venom and *Peganum Hermala* extract (at the same doses in protocol II and III), that were pre-incubated at room temperature (26±2°C) for 20 minutes before injection into the animals.

In protocol **V**, group E1 and E2 received only *Peganum Hermala* extract at doses of 15 mg/kg and 30 mg/kg, respectively. The intraperitoneal (IP) injection route was used in this study.
In protocol **VI**, group F1 and F2 and F3 received only *Peganum Hermala* extract at doses of 15, 30 and 60 mg/kg, orally respectively. The survival time of each animal (in minutes) after the injection or orally administrated of venom, extract, and venom/extract was recorded and statistically compared with the control groups.

Statistical analysis

The data are presented as mean ± SEM of survival time reported for each group. All the results were analyzed using SPSS-19 (SPSS Inc., Chicago, Illinois). One way analysis of variance (ANOVA) was used to analyze the data, followed by a post-hoc analysis using a Tukey test. The level of significance considered was $P < 0.05$.

Results

Protocol I, acute toxicity study

Group A, which is serve as control group, were was administered a dose of 10 mg/kg of *E. carinatus* venom alone. The mortality rate in this group was 100%, and the average time to death was 80 ± 5 minutes (Figure 2).

Protocol II, the effect of *Peganum Harmala* extract when injected simultaneously with the venom of *E. carinatus*

All mice in **Group B1 and B2** were treated with 15 and 30 mg/kg of *Peganum Hermala* extract respectively along with 10 mg/kg of venom simultaneously. In this group, the mortality rate was 100%, and the average time to death was 232 and 235 minutes respectively. These values were significantly different from the time to death of animals in Group A ($p<0.01$). (Figure **2**) (Table **1**).

Protocol III, the effect of *Peganum Harmala* extract when injected 20 min after the venom of *E. carinatus*

In this protocol, animals in Groups C1 and C2 received 15 and 30 mg/kg of *P. harmala* extract respectively, 20 minutes after being treated with 10 mg/kg of venom. The average time to death in these groups were 246 and 220 minutes

respectively, which were significantly different from the time to death of animals in Group A ($p<0.01$) (Figure **2**) (Table **1**).

Protocol IV, the effect of *Peganum Harmala* extract when mix with *E. carinatus* venom

In this protocol, group D1 and D2 were treated with a mixture 15 and 30 mg/kg of *P. Harmala* extract respectively and 10 mg/kg of venom which was incubated for 20 min prior to injection. The average time to death in these groups were 211 and 195 minutes respectively, which was significantly different from the time to death of animals in group A ($p < 0.01$) (Figure **2**) (Table 1).

Protocol V, effect of injection *Peganum Harmala* extract alone

In this protocol, group E1 and E2 were treated with only the *P. Harmala* extract at doses of 15 and 30 mg/kg, respectively (IP injection). All mice in these groups survived.

Protocol VI effect of orally administrated of *Peganum Harmala* extract alone

In this protocol, group F1, F2, and F3 were treated with only the *P. Harmala* extract at doses of 15, 30 and 60 mg/kg, respectively (orally). All mice in these groups survived (Table 1). This observation indicates a lack of toxic effects of the extract at the tested concentrations.

Discussion

There is currently no scientific research available regarding interaction between *P. harmala* and venomous animal venom particularly *E. carinatus* snake venom. The findings of this study demonstrated that the extract of *P. harmala* significantly antagonized the lethal effects of *E. carinatus* venom.

The statistical analysis showed that administering the plant extract at doses of 15 and 30 mg/kg alongside the venom significantly increased the average survival time

compared to the control group (P>0.05). It is important to note that this antagonizing effect was found to be independent of the extract concentration. Surprisingly, when the dose of the extract was increased from 15 to 30 mg/kg, the antagonizing effect actually reduced in groups C2 and D2.

The study indicated that although *P. harmala* extract did not fully neutralize the venom's lethality, but significantly increased the average survival time of the tested animals. The exact mechanism by which *P. harmala* counteracts the venom's lethal effects remains unclear, although various potential explanations have been investigated in research.

The extract of *P. harmala* is not toxic on its own at different dosage levels when tested through injection or oral administration. However, it has an antagonistic effect when combined with venom, suggesting it competes with the venom's molecular target. The exact mechanism is still unknown. It is important to note that *P. harmala* extract can be toxic when administered orally at higher doses [22], but the doses used in this study were enough to interfere with the venom's deadly effect.

The venom of *E. carinatus* demonstrates pronounced hemorrhagic and procoagulant properties. It consists of PLA2, hyaluronidase, and Zn2+ metalloprotease, all of which play a role in its life-threatening toxicity [4,16]. Snake venoms from the Viperidae, Hydrophiidae and Elaphidae families are a rich source of in phospholipase enzymes with remarkable functional diversity, responsible for a variety of pharmacological activities. These enzymes can rapidly hydrolyze phospholipids in cell membranes, such as those in erythrocytes and capillaries, resulting in the destruction of the circulatory system and causing bleeding [27]. They can also induce cardiotoxicity, myotoxicity, pre or postsynaptic neurotoxicity, edema, hemolysis, hypotension, convulsion and platelet aggregation [28].

The zinc-dependent metalloprotease found in viper venom including *E. carinatus* venom, disrupts the endothelial cells in blood vessels, resulting in spontaneous bleeding [29]. The combined action of metalloprotease and PLA2 in viper venom is responsible for the release of endogenous inflammatory mediators, local edema, and increased free radical formation at the bite site.

It is possible that the hemorrhagic activity of this venom is inhibited by the interaction of plant extract components with the metalloprotease and PLA2 activities or by the chelation of Zn^{2+} or Ca^{2+} ions; both of which are essential cofactors for these enzyme activity [30,31].

Previous research has shown that *Andrographis paniculata* and *Aristolochia indica* inhibit the hemolysis caused by *E. carinatus* venom in agarose-erythrocyte gels [32]. Moreover, *Horsfieldia amygdaline* is a plant from which PLA2 inhibitors have also been extracted [33].

Also, it has been reported that *Vitis vinifera* extracts were able to neutralize edema induced by the *E. carinatus* venom [34[. Similar action possibly took place with *P. harmala* extract, which contains numerous anti-inflammatory and active chemical constituents, including phenolic compounds and amino acids such as phenylalanine, valine, histidine, and glutamic acid. Additionally, it contains flavonoids like coumarin, tannins, sterols, and toxic alkaloids known as β-carbolines, which include Harmine, Harmaline, Harmol, and Harmalol [25,24].

It has been observed that β-carbolines have an affinity for different receptors such as serotonin, muscarinic, histamine, and benzodiazepine [35]. receptors therefore We can assume that the extract of *P. harmala* inhibits the specific receptors targeted by the active components present in the venom of *E. carinatus* which in turn, can potentially diminish the venom's lethal potency [35].

In addition to receptors, several studies suggest that the bioactive alkaloids, of *P. harmala* particularly harmaline and harmine, possess the capability to interfere with various enzymes. The primary mechanism of action of *P. harmala* involves the selective inhibition of the enzyme monoamine oxidase (MAO). MAO is responsible for the breakdown of crucial neurotransmitters, such as serotonin, dopamine, and norepinephrine [36].

As a result, it is possible that *P. harmala* also inhibits other enzymes, such as those found in the venom of *E. carinatus*, thereby reducing its lethal effects and significantly prolonging the time until animal death. However, it is imperative to substantiate this hypothesis through further experiments.

Some studies have found that certain snake venoms can block the release of acetylcholine and inhibit the neuromuscular junction [37]. Previous research has shown that substances from *P. harmala* seeds have inhibitory effects on acetylcholinesterase and butyrylcholinesterase. Inhibiting acetylcholinesterase can lead to the accumulation of acetylcholine, prolonging muscle stimulation and delaying paralysis [38]. However, more research is needed to understand the mechanisms at a molecular level.

Snake venom often exerts its toxicity through the generation of reactive oxygen species (ROS), leading to oxidative stress and tissue damage. *P. harmala* has been found to possess strong antioxidant properties, was purified and evaluated using a radical scavenging reagent, known as 2, 2-diphenyl-1-picrylhydrazyl (DPPH) solution. Harmal alkaloids (Harmine, Harmaline, Tetrahydroharmine) present in *P. harmala* exhibit anti-inflammatory and antioxidant effects that can effectively scavenge harmful free radicals. This ability to reduce oxidative stress, inflammation, and pain potentially contributes to its antivenom activity against *E. carinatus* venom [39].

Conclusion

In conclusion, our study determined demonstrates that the extract of *Peganum Harmala* demonstrates efficacy in effectively neutralizing neutralizes and delaying delays the lethal effects of *E. carinatus* venom, thereby offering protection against it. Consequently, it can be considered as an adjunctive therapy to complement conventional clinical treatments, particularly in situations where immediate access to healthcare facilities and anti-venom are unavailable. Future studies should prioritize the purification and characterization of the extract's potent components, as this may lead to the development of a novel chemical antidote for *E. carinatus* envenomation, enhance our understanding of the interactions between antagonistic components and the underlying mechanisms of action involved.

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Conflicts of interest

The authors have declared that there is no conflict of interest.

Ethics approval

The proposal and experiments were approved by the Animal Ethical Committee of our Faculty of Veterinary Medicine. (Ethics code IR.UM.REC.1401.171).

Authors' contributions

FB supervised, design the experiment and wrote the manuscript, revised and corrected it FB. SS and SF performed the experiments, collected data, analyzed and interpreted the results, and prepared the manuscript. All authors read, discussed, commented, and approved the final manuscript.

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Table 1. Application of different protocols and summary of the experiment results

Protocols	Groups	No of mice	venom mg/kg	*P. Harmala* mg/kg	Average time to death (min)
I	A	6	10	-	80
II	B1	6	10	15	232
II	B2	6	10	30	235
III	C1	6	10	15	246
III	C2	6	10	30	220
IV	D1	6	10	15	211

IV	D2	6	10	30	195
V	E1	6	-	15	Live
V	E2	6	-	30	Live
VI	F1	6	-	15/Po	Live
VI	F2	6	-	30/Po	Live
VI	F3	6	-	60/Po	Live

Protocols: **I,** Group A, only received venom at dose of 10 mg/kg (control).
Protocols: **II**, Groups **B1**& **B2**, received venom at 10 mg/kg along with *P. harmala* at 15 and 30 mg/kg (simultaneously).
Protocols: **III**, Groups **C1 & C2**, received venom at 10 mg/kg and *P. harmala* at 15 and 30 mg/kg respectively, after a 15-minute interval.
Protocols: **IV**, Groups **D1 & D2** received venom at 10 mg/kg along with *P. harmala* at 15 and 30 mg/kg incubated for 30 min prior to injection. The intraperitoneal (IP) route was used for injection.
Protocols: **V** Groups **E1 & E2** received only *P. harmala* at 15 and 30 mg/kg orally (IP).
Protocols: **VI** Groups **F1, F2 & F3** received only *P. harmala* at 15, 30 and 60 mg/kg orally (Po).

Figure 1: Viper snake *Echis carinatus, also called saw-scaled viper* (prepared by B. Fathi)

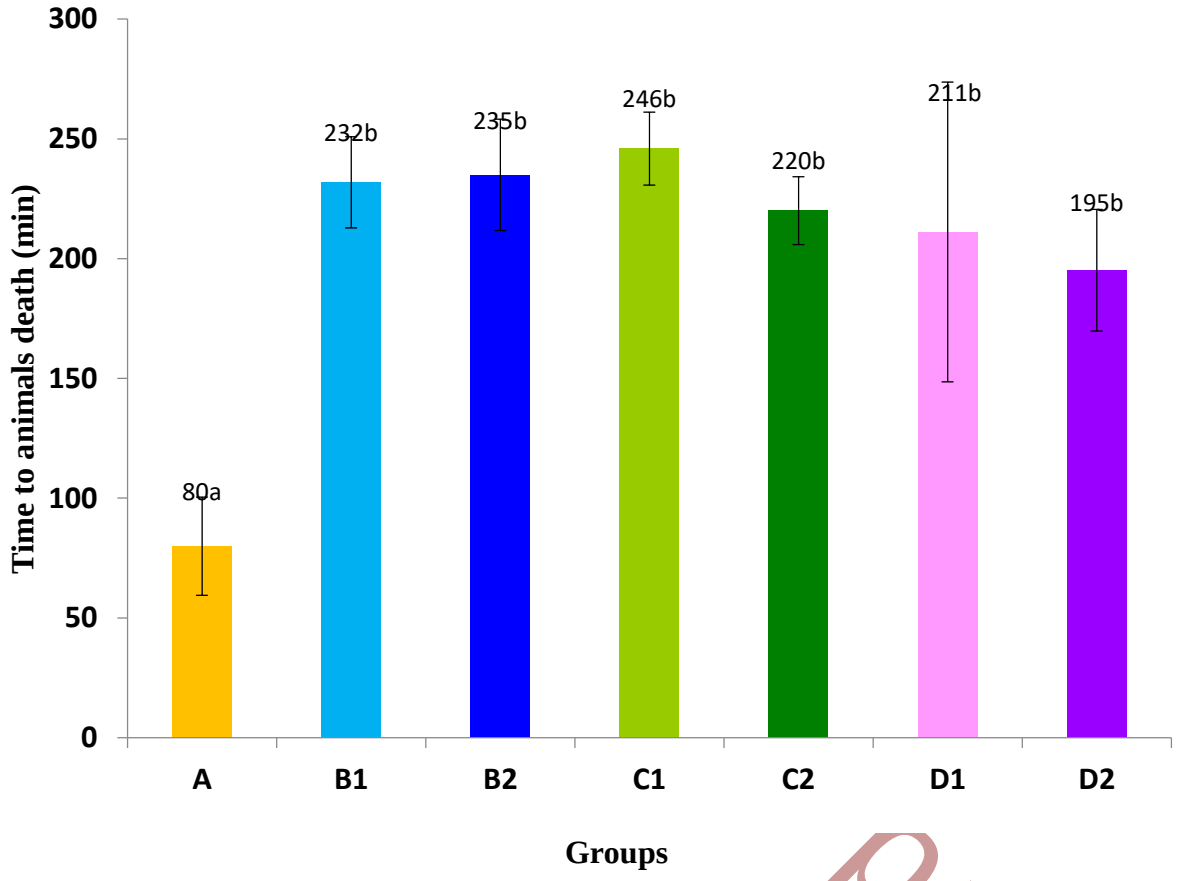

Figure 2: Display the Mean and standard deviation of the survival time for different treatments groups. Values that are followed by different superscript letters ($^{a, b}$) indicate a significantly difference at the level of ($P<0.05$).
Group A, received only venom at 10 mg/kg, Groups **B1**& **B2**, received venom at 10 mg/kg along with *P. harmala* at 15 and 30 mg/kg (simultaneously).

Groups **C1 & C2**, received venom at 10 mg/kg and *P. harmala* at 15 and 30 mg/kg respectively, after a 15-minute interval.

Groups D1 & D2 received venom at 10 mg/kg along with *P. harmala* at 15 and 30 mg/kg incubated for 30 min prior to injection. The intraperitoneal (IP) route was used for injection.

تاثیر مهاری عصاره گیاه اسپند، بر اثر کشنده زهر مار افعی جعفری در موش‌ها

دراین مطالعه تأثیرات آنتاگونیستی احتمالی عصاره گیاه اسپند (*Peganum harmala*) براثر کشنده زهر مار جعفری *E. carinatus* ارزیابی شده است. هفتاد و دو موش آلبینو به 12 گروه مساوی در 6 پروتکل آزمایشی تقسیم شدند. روش تزریق، داخل صفاقی بود. در پروتکل اول، به موش های گروه A (کنترل) به میزان 10 میلی‌گرم بر کیلوگرم زهربه تنهایی تزریق شد، آنها به طور میانگین بعد از 80 دقیقه تلف شدند. در پروتکل دوم، به گروه‌های B1 و B2 به ترتیب با 15 و 30 میلی‌گرم بر کیلوگرم عصاره گیاه اسپند با 10 میلی‌گرم بر کیلوگرم زهربطور همزمان تزریق شد. زمان زنده مانی آنها به ترتیب به 232 و 210 دقیقه افزایش یافت. در پروتکل سوم، به گروه‌های C1 و C2 ابتدا زهربا دوز 10 میلی‌گرم بر کیلوگرم تزریق شد و بعد از 15 دقیقه به ترتیب عصاره گیاه اسپند به میزان 15 و 30 میلی‌گرم بر کیلوگرم دریافت کردند. زمان مرگ آنها به ترتیب به 246 و 220 دقیقه افزایش یافت.

در پروتکل چهارم، به گروه‌های D1 و D2 محلول حاصل از انکوباسیون عصاره گیاه اسپند با زهربه مدت 30 دقیقه با دوزهای قبلی تزریق شد، زمان زنده مانی آنها به ترتیب به 211 و 195 دقیقه افزایش یافت. در پروتکل پنجم، گروه‌های E1 و E2 فقط عصاره گیاه اسپند را به میزان 15 و 30 میلی‌گرم بر کیلوگرم بصورت داخل صفاقی دریافت کردند. در پروتکل ششم، گروه‌هایF1 ، F2 و F3 فقط عصاره گیاه اسپند را به صورت خوراکی را و با دوزهای 15، 30 و 60 میلی‌گرم بر کیلوگرم به ترتیب دریافت کردند. آنها همه زنده ماندند. دراین مطالعه، گیاه اسپند به طور معنی‌داری ($p<0.05$) زمان زنده مانی موش ها را افزایش داد و بنابراین، دارای اثر آنتاگونیستی علیه اثر کشنده زهر مار جعفری می باشد و می‌تواند به عنوان یک کاندیدای ضد زهر برای تحقیقات بیشتر در نظر گرفته شود.

کلید واژگان: مار گزیدگی، مار جعفری، زهر، اسپند، اثرمخالف، موش ها