

## Evaluation of the Effectiveness of Tarantula Cubensis Extract in Cats Diagnosed with Stomatitis

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Received  
05.02.2025

Accepted  
19.03.2025

Published  
30.06.2025

DOI  
10.47027/duvetfd.1633969

**How to cite:** Türkarslan F, Tanrisever M, Ünsaldı E (2025). Evaluation of the effectiveness of tarantula cubensis extract in cats diagnosed with stomatitis. *Dicle Univ Vet Fak Derg.*, 18(1):13-18.

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### Abstract

Stomatitis in cats is an immune response to antigenic stimuli, exacerbated by viral infections. The etiopathogenesis of this disease, which manifests itself with sores in the mouth, has not been fully clarified. Today, in addition to medical treatment, partial or complete molar extractions are also performed. In this study, the results of using tarantula cubensis extract in addition to antibiotic treatment in the treatment of cats diagnosed with stomatitis at the Fırat University Animal Hospital Small Animal Surgery Clinic in Elazığ and the Hekimköy Veterinary Clinic in Adana were investigated. The cats were evaluated in two groups. The cats in the first group (ANT) ( $n=10$ ) received amoxicillin clavulanic acid treatment, and the cats in the second group (EXT) ( $n=10$ ) received tarantula cubensis extract injections in addition to the same antibiotic treatment. The response to the treatments was evaluated by 3 different surgeons, one week apart, by macroscopic inspection and scored between 1 and 4. The obtained data were statistically evaluated with the Mann Whitney U test and Wilcoxon tests. In this study, a statistically significant improvement was observed in cats treated with tarantula cubensis extract in addition to antibiotic treatment compared to cats treated with antibiotics alone.

**Key Words:** Cat, stomatitis, tarantula cubensis extract

### Stomatitis Tanısı Konan Kedilerde Tarantula Cubensis Ekstraktının Etkinliğinin Değerlendirilmesi

#### Öz

Kedilerde stomatitis antijenik uyarılara karşı, viral enfeksiyonlar ile şiddetlenen, bağışıklık sisteminin verdiği bir tepkidir. Ağız içerisinde çıkan yaralarla kendini gösteren bu hastalığın etiopatogenezisi tam olarak netlik kazanmamıştır. Günümüzde medikal tedavi yanı sıra kısmi veya tüm azı dişlerin çekimi de yapılmaktadır. Bu çalışmada, Elazığ'da Fırat Üniversitesi Hayvan Hastanesi Küçük Hayvan Cerrahi Kliniği'ne ve Adana'da Hekimköy Veteriner Kliniği'nde stomatitis tanısı konulan kedilerin tedavisinde antibiyotik tedavisine ek olarak tarantula cubensis ekstraktının kullanımının sonuçları araştırıldı. Kediler iki grup halinde değerlendirmeye alındı. Birinci gruptaki (ANT) kedilere ( $n=10$ ) amoksisilin klavulanik asit tedavi yapıldı, ikinci gruptaki (EXT) kedilere ( $n=10$ ) ise aynı antibiyotik tedavisine ek olarak tarantula cubensis ekstraktı enjeksiyonları yapıldı. Tedavilere verilen yanıt 3 ayrı cerrah tarafından, birer hafta arayla makroskopik yönden inspeksiyon ile değerlendirilerek ve 1 ile 4 arasında skorlandı. Elde edilen veriler istatistiksel açıdan Mann Whitney U testi ve Wilcoxon testleri ile değerlendirildi. Yapılan bu çalışmada antibiyotik tedavisine ek olarak tarantula cubensis ekstraktı ile tedavi edilen kedilerde, tek başına antibiyotik tedavisi yapılan kedilere kıyasla istatistiksel olarak anlamlı bir iyileşme olduğu görüldü.

**Anahtar Kelimeler:** Kedi, stomatitis, tarantula cubensis ekstraktı

## INTRODUCTION

Stomatitis in cats is a syndrome characterized by proliferative and ulcerative chronic inflammation of the soft tissues of the oral cavity (1). This syndrome is known by various names in the literature such as plasma cell stomatitis-pharyngitis (2), chronic gingivitis and pharyngitis (3), lymphocytic plasmacytic gingivitis-stomatitis (4), plasmacytic stomatitis-pharyngitis (5) and chronic stomatitis (6). It is a significant disease that causes pain in the oral cavity of cats and can be serious enough to lead to euthanasia of affected cats. The two main areas most difficult to treat are the tissue lateral to the palatoglossal folds and the mucosa covering the premolar/molar area extending into the buccal mucosa (7,8). It can also affect the pharynx, tongue and lips. Palatal inflammation can also be seen and periodontal lesions are often detected (9). Viruses associated with feline stomatitis include FIV, FHV-1, FCV and FeLV. Since the disease is very contagious, having many cats living in the same environment increases the risk factor considerably.

In cats with stomatitis, there are generally two treatment modalities: medical and surgical. Medical treatment alone usually does not yield positive results in the long term and may require surgical intervention; the current standard treatment method is tooth extraction. Regardless of the method, all treatment options require adequate pain management. Studies have shown that the extraction of some teeth (all premolars and molars) or the entire tooth gives good results in the long term (9-11). In the studies mentioned above, it was reported that approximately 70-80% of cats with stomatitis showed significant improvement, while approximately 20-30% of cats showed little or no improvement. Things you can do at home to treat this disease include brushing your cat's teeth or using oral antiseptics containing chlorhexidine (12,13). The goal of treatment for feline stomatitis has been to suppress the immune system because this disease is an immune-mediated inflammatory disease (14). In cases of feline stomatitis, antibiotic treatment alone provides only temporary relief (13,15). Commonly recommended antibiotics include amoxicillin/clavulanic acid, metronidazole, clindamycin, and doxycycline. Antibiotic treatment is recommended, which can last from a week to months, and sometimes it can be combined with topical treatment (12-15).

Corticosteroids are used in feline cases of stomatitis due to their immunosuppressive and anti-inflammatory effects (7,15,16). Azathioprine, chlorambucil and cyclophosphamide are other immunosuppressive drugs used (16,17). Additionally, nonsteroidal anti-inflammatory drugs (NSAIDs) are often recommended along with antibiotic treatment in cats with stomatitis (7,18). The purpose of this study was to investigate the effectiveness of tarantula cubensis extract, which can be used in addition to antibiotic treatment in cats with stomatitis.

## MATERIAL AND METHODS

The material of this study consisted of cats with stomatitis that were brought to Firat University Animal Hospital Small Animal Surgery Clinic in Elazığ and Hekimköy Veterinary Clinic in Adana with the complaint of sores in the mouth. Cats

of different species, breeds, sex, age and weight were brought to the clinic and treatment was started without any selection. These cats with stomatitis brought to the clinic were evaluated for renal failure and such cats with stomatitis were excluded from the study. In addition, overweight obese cats and underweight cats were also excluded from the study. In cats with stomatitis brought to the clinic, the mouth area was firstly antisepticized. During the treatment period, cats in the first group (antibiotic group  $n=10$ ) (ANT) received routine antibiotic treatment with amoxicillin/clavulanic acid, 8.75 mg/kg intramuscularly (Synulox, 140 mg amoxicillin trihydrate and 35 mg clavulanic acid, Haupth Farma, Italy) for 10 days. In the second group (extract group  $n=10$ ) (EXT), in addition to the same dose of antibiotic, subcutaneous tarantula cubensis extract (tarantulacubensis D6 1ml in 1ml) (Theranekron D6, Richter Pharma, Austria) 0.5-1ml was administered subcutaneously 2-3 times at 1 week intervals. In addition, a mouth spray (Klorhex Plus, Drogosan, Turkey) containing 0.075 g flurbiprofen and 0.036 g chlorhexidine digluconate was used as oral antiseptic for all cats. For the ANT group, antibiotics were administered for 1 week, followed by a 1-week break, and then continued again for 1 week with a daily dose, while the patient owners were instructed to use the mouth sprays regularly in both groups. During this treatment period, intraoral photographs were taken regularly for later evaluation. Healing rates were evaluated macroscopically by 3 different surgeons at one week intervals and scored between 1 and 4. These values were transferred to a table and evaluated statistically.

## Statistical Analysis

IBM SPSS Statistics 22 program was used in the statistical analysis of the study. The normality of the parameters was determined by the Shapiro-Wilk test and it was understood that they did not show a normal distribution. The Mann-Whitney U test was used to compare quantitative data between two groups.

The Friedman test (post hoc Wilcoxon signed-rank test) was used to evaluate within-group changes. Statistical significance was considered at the  $P<0.05$  level.

## RESULTS

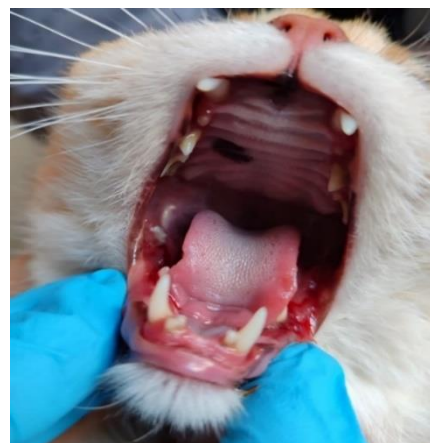
Cats with stomatitis brought to the clinic with the complaint of wounds in the mouth area were evaluated in two separate groups, while the cat owners in both groups were told to bring their cats to the clinic for examination and further treatment at one-week intervals. All patient owners were given the necessary information about the treatment process; antibiotic administration, use of oral antiseptics and nutrition with soft foods. In addition, for cats to be treated with tarantula cubensis extract, their owners were informed in detail about the subject and this extract was applied only in the clinic. Cats with an average body weight of 3-4 kg were included in the study. At the end of the study, the pictures obtained on the 1st, 7th, 14th and 28th days were subjected to macroscopic evaluation by three different surgeons without knowing which group they belonged to (Figure 1-5).



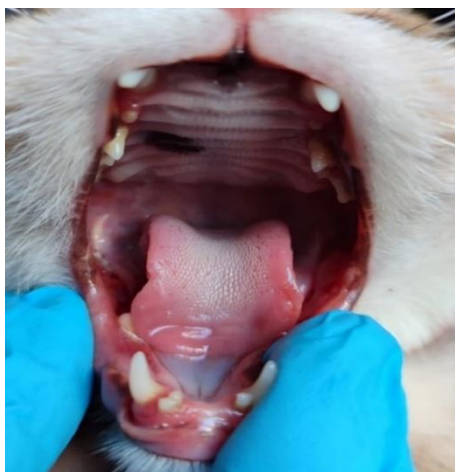
**Figure 1.** Lesions extending around the mouth of cat number 1 belonging to ANT group (7th day)



**Figure 2.** Regression of stomatitis-related lesions in cat number 1 of ANT group (day 21)



**Figure 3.** Appearance of intraoral lesions in cat number 4 belonging to the EXT group (7th day)



**Figure 4.** Improvement in the intraoral lesions of cat number 4 belonging to the EXT group (28th day)



**Figure 5.** Healing status of cat no. 5 in ANT group between day 1 and day 28

The assessments were scored, with 1 being the worst and 4 being the best, and then averaged. The values obtained were recorded in a table (Table 1, Table 2, Table 3). It was evaluated that there was no visible improvement in the first two weeks in both groups (Figure 1, Figure 3). Differences between the groups in terms of Healing Scores were given in Table 4.

**Table 1.** Healing rates of ANT group cats (1 represents the worst healing, 4 represents the best healing)

Cat No	1st day	7th day	14th day	28th day
Cat 1	1	1	2	3
Cat 2	1	1	2	2
Cat 3	1	2	3	3
Cat 4	1	1	2	2
Cat 5	1	1	3	4
Cat 6	1	1	2	3
Cat 7	1	1	2	2
Cat 8	1	2	2	2
Cat 9	1	1	2	2
Cat 10	1	1	2	2

**Table 2.** Healing rates of EXT group cats (1 represents the worst healing, 4 represents the best healing)

Cat No	1st day	7th day	14th day	28th day
Cat 1	1	2	2	3
Cat 2	1	1	2	3
Cat 3	1	2	3	3
Cat 4	1	2	2	3
Cat 5	1	2	3	3
Cat 6	1	1	2	3
Cat 7	1	2	3	4
Cat 8	1	1	2	3
Cat 9	1	1	2	2
Cat 10	1	2	3	4

**Table 3.** Table containing the mean values of the groups (1 indicates the worst healing; 4 indicates the best healing)

Group	1st day	7th day	14th day	28th day
ANT group	1.00	1.20	2.20	2.50
EXT group	1.00	1.50	2.40	3.10

**Table 4.** Evaluation of Healing Scores Between Groups

		1st day	7th day	14th day	28th day
<b>ANT</b>	Min-Max	1-1	1-2	2-3	2-4
	Mean $\pm$ SD (Median)	1 $\pm$ 0 (1)	1.2 $\pm$ 0.4 (1)	2.2 $\pm$ 0.4 (2)	2.5 $\pm$ 0.7 (2)
<b>EXT</b>	Min-Max	1-1	1-2	2-3	2-4
	Mean $\pm$ SD (Median)	1 $\pm$ 0 (1)	1.6 $\pm$ 0.5 (2)	2.4 $\pm$ 0.5 (2)	3.1 $\pm$ 0.6 (3)
	P	1.000	0.075	0.342	0.042*

Mann Whitney U test \*P&lt;0.05

There was no statistically significant difference between the groups in terms of day 1, day 7 and day 14 healing levels (P>0.05). The 28th day healing score of the EXT

group was statistically significantly higher than the ANT group (P:0.042; P<0.05). (Table 5)

**Table 5.** Evaluation of intra-group healing scores

	<b>ANT</b>		<b>EXT</b>	
	Min-Max	Mean $\pm$ SD (Median)	Min-Max	Mean $\pm$ SD (Median)
<b>Day 1</b>	1-1	1 $\pm$ 0 (1)	1-1	1 $\pm$ 0 (1)
<b>Day 2</b>	1-2	1.2 $\pm$ 0.4 (1)	1-2	1.6 $\pm$ 0.5 (2)
<b>Day 3</b>	2-3	2.2 $\pm$ 0.4 (2)	2-3	2.4 $\pm$ 0.5 (2)
<b>Day 4</b>	2-4	2.5 $\pm$ 0.7 (2)	2-4	3.1 $\pm$ 0.6 (3)
<sup>1</sup> p		0.001*		0.001*
<b>Day 1-Day 7 <sup>2</sup>p</b>		0.157		0.014*
<b>Day 1-Day 14 <sup>2</sup>p</b>		0.003*		0.004*
<b>Day 1-Day 28 <sup>2</sup>p</b>		0.004*		0.004*
<b>Day 7-Day 14 <sup>2</sup>p</b>		0.004*		0.005*
<b>Day 7-Day 28 <sup>2</sup>p</b>		0.006*		0.004*
<b>Day 14-Day 28 <sup>2</sup>p</b>		0.083		0.008*

<sup>1</sup>Friedman Test <sup>2</sup>Wilcoxon sign test \*P<0.05

In the ANT group, the changes observed in the healing scores across the days were statistically significant (P:0.001; P<0.05). No significant change was observed in the healing scores from day 1 to day 7 (P>0.05); however, the increases in healing scores from day 1 to day 14 and day 28 were statistically significant (P<0.05). The increases in healing scores from day 7 to day 14 and day 28 were statistically significant (P<0.05). No significant change was observed in the healing scores from day 14 to day 28 (P>0.05).

In the EXT group, the changes observed in the healing scores across the days were statistically significant (P:0.001; P<0.05). The increases in healing scores from day 1 to day 7, day 14, and day 28 were statistically significant (P<0.05). The increases in healing scores from day 7 to day 14 and day 28 were statistically significant (P<0.05). The increase in healing scores from day 14 to day 28 was statistically significant (P<0.05) (Table 6, Chart 1).

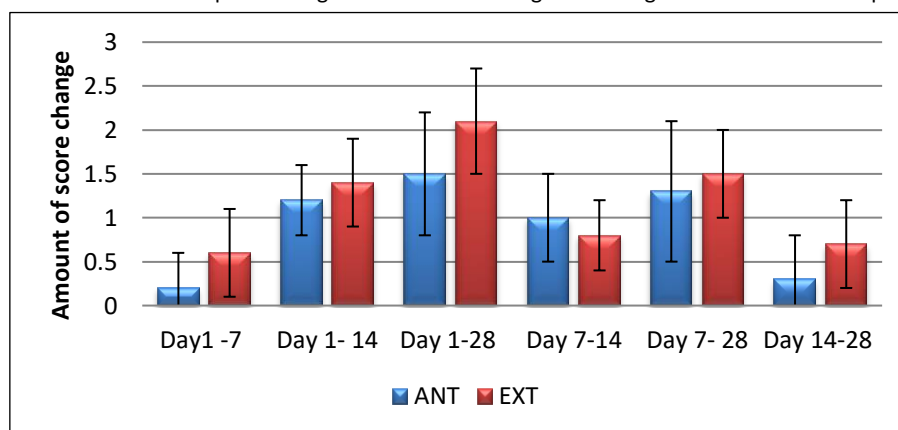
**Table 6.** Evaluation of the Changes in Healing Scores Between Groups

	<b>ANT</b>		<b>EXT</b>		
Changes	Min-Max	Mean $\pm$ SD (Median)	Min-Max	Mean $\pm$ SD (Median)	p
<b>Day 1-7</b>	0-1	0.2 $\pm$ 0.4 (0)	0-1	0.6 $\pm$ 0.5 (1)	0.075
<b>Day 1-14</b>	1-2	1.2 $\pm$ 0.4 (1)	1-2	1.4 $\pm$ 0.5 (1)	0.342
<b>Day 1-28</b>	1-3	1.5 $\pm$ 0.7 (1)	1-3	2.1 $\pm$ 0.6 (2)	0.042*
<b>Day 7-14</b>	0-2	1 $\pm$ 0.5 (1)	0-1	0.8 $\pm$ 0.4 (1)	0.329
<b>Day 7-28</b>	0-3	1.3 $\pm$ 0.8 (1)	1-2	1.5 $\pm$ 0.5 (1.5)	0.396
<b>Day 14-28</b>	0-1	0.3 $\pm$ 0.5 (0)	0-1	0.7 $\pm$ 0.5 (1)	0.081

Mann Whitney U test \*P&lt;0.05



Chart 1. Graph Showing the Amount of Change in Healing Scores Between Groups



There was no statistically significant difference in the amount of increase in healing scores on day 7 compared to day 1 between the groups ( $P>0.05$ ). Similarly, there was no statistically significant difference in the amount of increase in healing scores on day 14 compared to day 1 between the groups ( $P>0.05$ ). The increase in healing scores on Day 28 compared to Day 1 in the EXT group was statistically significantly higher than in the ANT group ( $P:0.042$ ;  $P<0.05$ ).

There was no statistically significant difference in the amount of increase in healing scores on day 14 compared to day 7 between the groups ( $P>0.05$ ). Similarly, there was no statistically significant difference in the amount of increase in healing scores on day 28 compared to day 7 between the groups ( $P>0.05$ ). There was no statistically significant difference in the amount of increase in healing scores on day 28 compared to day 14 between the groups ( $P>0.05$ ).

## DISCUSSION AND CONCLUSION

Stomatitis in cats is unfortunately a serious and frustrating disease that is poorly defined in the literature. This disease not only causes pain and stress for the cat, but also creates a very worrying situation for cat owners due to inadequate response to various treatments. Studies have investigated the possible causes of stomatitis in cats; however, its exact etiopathogenesis remains unclear. The related pathogens include bacteria and viruses, but immune-related causes have also been proposed. In this study, the effectiveness of Tarantula cubensis extract in treatment, in addition to antibiotic therapy, was investigated.

Taskaya et al. (19), in a study they reported that there was no statistically significant difference between the two drug groups (amoxicillin 7 mg + clavulanic acid 1.75 mg, subcutaneously, mg/kg body weight or trimethoprim 4 mg + sulfadimethoxine 20 mg, subcutaneously, mg/kg body weight) used in the treatment of stomatitis in cats. In this study, amoxicillin-clavulanic acid treatment was applied to one group, while the other group received Tarantula cubensis extract in addition to this treatment protocol. The results showed that a statistically significant difference emerged between the groups in terms of treatment effectiveness.

Jennings et al. (11), in a retrospective case series involving 95 cats with stomatitis who were treated with full or partial tooth extractions along with concurrent medical management, reported that 28.4% of the cats experienced complete healing, 39% showed significant clinical healing, 26.3% had minimal healing, and 6.3% showed no healing. In

a more recent study by Druet and Hennet (10), 56 cats treated with tooth extraction were reported, with 51.8% of the cats achieving clinical improvement or significant improvement within an average of 38 days. Hennet *et al.* (7), in a study they conducted, reported that 23% of 11 cats treated with prednisone showed significant improvement, and 7% achieved clinical improvement.

Vercelli et al. (20), in their study, investigating the effectiveness of oral cyclosporine in 8 cats that had not previously been treated with tooth extractions, reported that 4 cats (50%) achieved clinical remission, and the remaining cats showed considerable improvement.

Lommer (21), shows that in his study, applied oral cyclosporine to 9 cats previously treated with extractions. He stated that after 6 weeks, there was a 77.8% healing in the treated cats and a 14.3% healing in the placebo group, which was statistically significant. Long-term observation was conducted on 11 cats, and it was reported that 5 of them (45.5%) showed clinical improvement after receiving cyclosporine for 3 months or longer.

Arzi et al. (22), in a study they conducted, treated 7 cats with autologous adipose-derived mesenchymal stem cells. They reported a 71.4% positive response rate, with clinical remission observed in 42.8% of the cats. Additionally, they mentioned that 28.6% of the cats showed no significant improvement.

Albay et al. (23), in a study they conducted, evaluated the effectiveness of Tarantula cubensis extract (1:100/D2, Theranekron®, Richter Pharma, Austria) in treating oral lesions in bovine blue tongue disease. A total of 9 patients were treated, with 6 cattle receiving tetracycline, flunixin meglumine, and Tarantula cubensis extract (Theranekron), while the remaining 3 cattle were treated as controls with the same treatment regimen excluding Theranekron. Twenty-four hours later, the treatment group showed faster re-epithelialization and return to normal body temperature compared to the control group. In this study, the application of Tarantula cubensis extract in addition to antibiotic therapy in 10 out of 20 cats resulted in statistically significant healing. This study is in parallel with the current study.

In conclusion, it was determined that the application of Tarantula cubensis extract, in addition to current treatments, may be relatively effective in the regeneration of oral and surrounding wounds in the treatment of stomatitis, a chronic, non-healing disease in cats.

## ACKNOWLEDGEMENT

This article has been produced from a master's thesis. We would like to thank everyone who contributed to the completion of this study.

## FINANCIAL SUPPORT

No support was received from any organization in the conduct of this research.

## CONFLICT OF INTEREST

There is no conflict of interest to be declared by the authors.

## AUTHOR CONTRIBUTIONS

MT, EÜ and FT took part in the planning of the study and the collection of sample images. Clinical studies were conducted by MT, EÜ and FT. The writing and final checks of the study were carried out with the contributions of all authors.

## ETHICAL STATEMENT

This study was approved by Firat University (Protocol Number: 21564 and date: 17.01.2024) Local Animal Experiments Ethics Committee.

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