Original Article https://doi.org/10.47748/tjvr.1226644

TJVR 2023; 7 (1): 39-45

Turkish Journal of Veterinary Research

https://dergipark.org.tr/tr/pub/tjvr

e-ISSN: 2602-3695

The therapeutic effectiveness of thyme extract in naturally infected puppies with ascariasis

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Received: 30.12.2022 Accepted: 28.02.2023

ABSTRACT

Objective: This study aimed to investigate the therapeutic efficacy of thyme extract in puppies naturally infected with ascarids.

Material-Method: The study consisted of 20 puppies of different sexes, 2-4 months old, naturally infected with ascarid. There were given an oral 20% concentration of thyme extract for 3 days to puppies, and faecal egg counts were conducted on the 0th, 1st, 2nd, 3rd, and 7th days after the treatment was started (day 0). Also, serum urea, creatinine, AST, ALT levels were monitored on the 0th and 3rd days, together with daily clinical examination, to monitor possible toxic effects.

Result: In 2 puppies (10%), the fecal egg count was highly variable at post-treatment examinations, but no reduction in egg count was observed. Egg shedding in 7 (35%) of the treated puppies was zero. It was observed that egg shedding was not completely zero in 11 of the puppies (55%). However, the egg counts decreased by 25% to 98.3%. It was also observed that the values of the measured blood biochemical values were within reference range except serum urea levels and the puppies did not show any clinical sign of toxicity during the treatment.

Conclusion: It was concluded that the thyme extract did not have any toxic effect in the puppies at the concentration studied, and it could be effective in the treatment of ascariasis.

Keywords: *Toxocara spp., Puppy, Ascariasis, Treatment, Thyme extract*

INTRODUCTION

Ascarids are among the most common gastrointestinal parasites encountered in dogs (Overgaauw and Van Knapen, 2013; Becskei et al., 2020a). Globally, *Toxocara canis* and *Toxascaris leonina* in particular, are the most common canine ascarids (Becskei et al., 2020b). These parasites, which settle in the small intestines of their main hosts, carnivores can also infest paratenic hosts such as; humans, mice, earthworms, ticks, chickens, sheep, pigs and birds (Glickman and Schantz, 1981). Ascarids are important zoonoses because they can be easily transmitted to humans from cats and dogs with whom we are in constant contact in our daily lives (Despommier, 2003).

The development and course of the infection in dogs; the age, sex of the animal, the number of infected eggs exposed, hormonal status, immune system and the migration route of the larvae

directly affect it (Lloyd et al., 1998). It can cause growth retardation, diarrhoea, dehydration, abdominal bloating, intestinal obstruction, ascarid toxicity and death, especially in young dogs (Burrows et al., 1995).

In the fight against ascariasis in dogs, it is recommended to first deworm puppies from parasites, and then apply ascarid treatment to adult dogs four times a year, even if there is no effective and regular examination (Becskei et al., 2020b). Due to its zoonotic importance, it has been reported that dogs that come into contact with individuals with compromised immune systems should be treated monthly (Companion Animal Parasite Council, 2020). In the treatment of ascariasis in dogs, medications such as; pyrantel pamoate, ivermectin, selamectin, eprinomectin, moxidectin, nitroscanate, mebendazole, milbemycin, sarolaner, spinosad, lotilaner, praziquantel are used either alone or in combinations (Genchi et al., 1990; Clark et al., 1991; Bowman et al., 1998; McTier et al., 2000; Kozan et al., 2008; Cardenas et al., 2017; Young et al., 2021). However, there is no 100% effective treatment protocol for *T. canis* in dogs, since its biology is very complex and there are still aspects of it that cannot be clarified (Doğanay et al. 2018).

In its simplest form, phytotherapy can be defined as the treatment made with plants. Phytotherapy, together with chemical treatments or as an alternative treatment, has attracted the attention of researchers in recent years (Sarışen and Çalışkan, 2005). When the phyto-therapeutic potentials of thyme were examined; it was reported to have antibacterial, antiviral, antiparasitic, antifungal and antioxidant potentials (Burt, 2004). The essential oils of thyme contain compounds such as; carvacrol, borneon, tanen, pimen, cymol, and flavones in addition to their intense thymol quantity. Their thymol ratio is around 50% (Benli and Yiğit, 2005).

In this study, it was aimed to investigate the treatment efficacy of thyme extract as an alternative to chemical treatments in naturally infested puppies with ascarid.

MATERIALS and METHODS

The study was carried out with the permission of Kırıkkale University Animal Experiments Local Ethics Committee, dated 19/12/2019 and numbered 63. The study consisted of 20 puppies of different sexes, 2-4 months old, which were brought to Kırıkkale University, Veterinary Faculty, Animal Hospital for medical examination and vaccination. Puppies that were mono-infected with ascaris upon stool examinations were included in the study.

Before the administration of thyme to the animals included in the study, blood and stool samples were taken, it was administered to orally 3 times in total on the 0^{th}, 1^{st} and 2^{nd} days, by diluting the commercial thyme extract (Thy717, BioArt, Turkey) to a concentration of 20%, at a dose of 1 ml/kg.

Stool samples were taken from the puppies for a total of 5 times, on the first 4 days and on the 7^{th} day of the beginning of the treatment, to count eggs in each gram faeces. In order to monitor for possible toxicity; serum urea, creatinine, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values were measured by taking blood samples twice, before thyme extract administrations (day 0) and after thyme extract administrations (3th day).

To determine the presence of *Toxocara* spp. eggs in stool samples, the Fülleborn flotation technique was used. The Mc Master technique was adopted to determine the number of eggs in 1 g stool before, during, and after the treatment. For this, the average of 40 glass beads were thrown into 100 ml jars. Three g of faeces was weighed and put into the jar and 42 ml of saturated salt water was added. Stool was homogenized by closing the lid of the jar. The resulting solution was transferred into centrifuge tubes and centrifuged at 1500 rpm for 3 minutes. The upper liquid was removed without moving the sediment at the bottom, and the same amount of saturated salt water was added to the faecal residue at the bottom of the tube, and the centrifuge tube was turned upside down 5-6 times to homogenize the sediment. The chambers of the Mc Master slide were filled with the help of a Pasteur pipette. Eggs were counted at x10 magnification under the light microscope and the number of eggs detected in both chambers was multiplied by 100 to determine the total number of eggs in 1 gram of stool (Şenlik, 2006). Faecal egg reduction test (FECRT) was also adopted to determine the efficacy of the thyme extract against *T. canis* (Doğanay et al., 2018). Egg reduction was calculated according to the formula below.

$$\text{FECRT} = \frac{\text{EPG value before treatment - EPG value after treatment}}{\text{EPG value before treatment}} X100$$

RESULTS

The daily change in *Toxocara* spp. egg counts in the puppies given the thyme extract is presented in Table 1. According to the data, it was determined

that the number of eggs was zeroed after the administration of the thyme extract in 7 out of 11 puppies which had faecal egg counts between 200 and 1650 on day 0, and in 1 out of 9 puppies which had faecal egg counts more than 1650. In total, faecal egg counts zeroed in 7 dogs (35%).

There was no decrease in the number of eggs laid in 2 of the 20 puppies. In 11 puppies, the egg laying rate showed a wide distribution between 25% and 98.3% (Table 1). Considering the general distribution, the percentage of egg reduction was found to be higher in puppies with relatively low egg counts prior to treatment.

Table 1. Faecal egg counts results of the puppies

No.	Day 0	Day 1	Day 2	Day 3	Day 7	% of Reduction
1	200	0	0	0	0	100
2	200	700	400	0	0	100
3	500	0	0	200	0	100
4	500	Not Sampled	50	0	250	50
5	500	150	0	0	50	90
6	750	Not Sampled	0	0	50	93.3
7	1000	900	1350	5200	3700	No Reduction
8	1100	7450	0	0	0	100
9	1500	1650	1200	1250	0	100
10	1500	Not Sampled	0	100	900	40
11	1650	Not Sampled	700	50	0	100
12	2100	1950	4950	9800	4600	No Reduction
13	2350	3900	5000	6000	1150	51.1
14	2500	4100	7100	6000	1050	58
15	3000	3000	2350	500	50	98.3
16	4250	12000	11650	0	0	100
17	8400	5800	1200	4000	6300	25
18	8400	5100	6250	12150	6050	28
19	15000	18200	2700	6250	1450	90.3
20	28150	5050	9600	16250	17900	36

Table 2. Mean changes in blood biochemical parameters before and after treatment.

Parameters	Before Treatment (n=20)			After Treatment (n=20)			Reference Values
	Min	Max	$\bar{x}$	Min	Max	$\bar{x}$	
Urea (mg/dl)	10	28	15.38	13	57	24.52	10-26
Creatinine (mg/dl)	0.16	0.48	0.26	0.12	0.57	0.32	0.5-1.3
AST (U/L)	15	88	28.84	7	58	21.15	10-88
ALT (U/L)	9	21	15.15	3	26	15.63	10-90

An adult worm was detected on the 7th day after the treatment in puppy number two and on the 3rd day in puppy number 10. On the 3rd day after the treatment, a large number of adult parasite excretions were observed in dogs with 17 and 19 numbers. It was observed that the general condition of dog number 15 was deteriorated prior to the treatment, however, the general condition improved after 3 days of treatment.

The mean values obtained from the measurements made from the blood samples taken before and after the treatment are given in Table 2. It was observed that serum urea, creatinine, AST and ALT values in the blood samples taken 24 hours after the last treatment dose were within the normal reference ranges. Although the mean value of urea after treatment approached the upper limit, it was still within the normal reference limit.

All the animals included in the study were clinically completely healthy during the study and on the 7th day examinations. During this period, there were no findings such as diarrhoea, vomiting, depression and anorexia that could indicate clinical toxication.

DISCUSSION

Canine ascariasis can cause fatal diseases, especially in susceptible dogs, and draws attention as it is a zoonotic condition (Macpherson, 2013; Hassanain et al., 2015). Especially in areas where people and dogs are in close contact, such as parks and gardens, the parasite can easily be transmitted to both susceptible dogs and humans by faecal contamination (Fankhauser et al., 2016). For this reason, in the fight against ascariasis in dogs, it is recommended to break the parasitic cycle by spraying dogs at least 4 times a year, even if no parasite is found (Becskei et al., 2020b). Due to widespread resistance to anti-helminthics (chemical drugs) used in the treatment of canine ascariasis, there is the need to constantly seek for new remedies (Coles et al., 1992; Hoekstra et al., 1997; Silvestre and Humbert, 2002). Among the strategies developed against helminths is phytotherapy (Jahangir et al., 2001).

Considering studies investigating the antiparasitic activities of thyme: Hafez et al. (2019) and Amin et al. (2016) *T. canis* in experimentally infected rats; Amin and El-Kabany (2013), *T. vitulorum*; Luis et al. (2016) anti-helminthic against *Haemonchus contortus* in experimentally infected sheep; Malatyalı et al. (2009) antileishmanial in vitro; Behnia et al. (2008) *Entamoeba histoytica* trophozoites in vitro; Gaur et al. (2018) in cell culture, Kara et al. (2022) anti-protozoan on *Cryptosporidium parvum* in experimentally infected rats; Attia et al. (2015), intestinal and cystic stages of *Trichinella spiralis*; Morsy et al. (1998) *Lucilia sericata* larvae; Remmal et al. (2011), Abbas et al. (2012), Arczewska-Wlosek and Swiatkiewicz (2012) studied the anticoccidial activity of thyme.

Studies have shown that the ant-parasitic activity of thyme extract is mediated by thymol, which constitutes 50% of the active ingredients (Ferreira et al., 2016). It has been reported that the anti-helmintic effect of tymol is based on its paralysing of the parasite, similar to the mechanism of action of macrocyclic lactones, and the inhibition of movement and feeding functions (Kotze et al., 2012; Lynagh et al., 2014). It has been reported that when macrocyclic lactones such as ivermectin, moxidectin, and eprinomectin are used for treatment in canine ascariasis, it reduces the number of faecal eggs by 100%, while this rate is 99.7% with topical use of selamectin, a member of the same group (Pal et al., 1995, Gargılı et al., 1999; Payne- Johnson et al., 2000; Kozan et al., 2008). Despite its success in treatment, it should not be forgotten that ivermectins are neurotoxic, especially in sensitive breed dogs such as Collies (Pronk and Schefferlie, 1998).

In canine ascariasis, both the toxic/side effects of chemical agents and the development of antiparasitic resistance, and the costs of continuous new drug development have led researchers to seek for treatment options (Pronk and Schefferlie, 2022; Jackson and Miller, 2006). Hassanain et al. (2015) compared the efficacy of mebendazole and sugar lemon (*Citrus aurantifolia Swingle*) seed extract in dogs naturally infected with *Ancylostoma caninum* and *T. canis*. According to the study, the number of faecal eggs was taken as a reference in the evaluation of treatment efficacy, faecal egg numbers; decreased by 74.10% in the group given only mebendazole, by 91.08% in the group given only sugar lemon extract, and by 98.20% in the group given mebendazole and sugar lemon extract. In our study, egg laying decreased by 25-100% in 18 dogs given thyme extract, while egg laying did not decrease in 2 dogs.

Amin et al. (2016) evaluated the therapeutic efficacy of thyme oil in experimentally infected rats with *T. canis*; they took the number of larvae detected in the brain tissue and brain damage as success criteria and reported that the treatment with thyme oil was found to be effective compared to the control groups. Hafez et al. (2019) examined the therapeutic efficacy of thyme oil in rats experimentally infected with *T. canis* larvae in a similar study. In the evaluation of the efficacy of the treatment, the histological changes observed in the testis tissue due to larval migration were taken as reference; while moderate and reversible changes were observed in the testicular tissue of the group treated with the thyme oil, serious histopathological changes were detected in the control group. In both studies, thyme oil was found to be effective in the treatment of experimental *T. canis* infection in rats. This result obtained in the experimental animals inspired this clinical study in dogs, the definitive host of *T. canis*.

In our study, it was determined that the number of eggs in the faecal samples taken 24 hours after the first treatment application increased significantly. This is thought to be due to increase intestinal peristalsis of thyme extract, induced fragmentation of adult parasites and increase in the number of eggs excreted in faeces due to fragmentation of adult female parasites.

Yıldız et al. (2011) in a study in which they examined the efficacy of *Artemisia absinthium* extract in cats naturally infected with *Toxocara cati*, they reported that egg laying stopped in only two of the 8 cats given the extract, and in the remaining cats, although the number of eggs decreased compared to the first day, the laying did not stop. In our study, egg laying stopped in 8 dogs (40%) after the administration of the thyme extract against *T. canis*, which is in the same family as *T. cati*. Similar to the related study, in 3 dogs egg shedding was reduced by 90.3-98.3%, while there was no decrease in 2 dogs. In 7 dogs, egg laying decreased by 25-58%. When the results of these studies were compared, it was found that the zeroing rate of thyme extract (35%) was higher compared to the zeroing rate of *A. absinthium* extract against ascarides (25%).

Hassanain et al. (2015) applied *Citrus aurantifolia* (lemon blossom) extract against *T. canis* in Egypt. In that study, they reported that the number of eggs decreased by 91.8% in the group in which only *C. aurantifolia* was administered. In our study, when the egg reduction in the stools examined before and after the treatment was calculated, it was determined that the egg reduction varied individually in the animals and the egg reduction was between 25-100%. In addition, it was recorded in 2 dogs that thyme extract had no effect on the number of eggs excreted in the faeces.

Although some of the cat and dog owners believe that natural products are safer than synthetic chemicals in parasitic control, it should not be forgotten that essential oils and plant extracts also have toxic effects on animals (Villar et al., 1994; Woolf, 1999; Genovese et al., 2012). Genovese et al. (2012), in their retrospective study covering a 2-year period, in which they compiled the cases of poisoning reported as a result of the use of topical products containing essential oil in cats and dogs; they evaluated different products made of oils such as peppermint, cinnamon, lemongrass, clove, thyme, cedarwood, rosemary, wheat germ oil. In the evaluation, clinical findings such as lethargy, weakness, desire to lie down, hyperactivity, tachycardia, hypothermia, hyperthermia, seizures, skin erythema, vomiting, diarrhea, edema, ataxia, agitation, anorexia, fasciculation, hiding, hypersalivation, panting, tremor were observed in animals. They mentioned that kidney failure may occur. Bischoff and Guale (1998) reported that liver enzymes such as ALT and AST increased in cats exposed to tea tree (*Melalleuca alternifolia*) oil poisoning. In this study, in which ascariasis was treated with the oral use of thyme extract, no clinical symptoms of poisoning were observed during or after the study. In order to monitor whether the treatment with thyme extract caused organ failure or not, urea and creatinine were measured for kidney failure, and AST and ALT values were measured for liver failure. Although all values before and after treatment were within their normal physiological reference limits, it was noted that the urea value approached the upper reference values after treatment. In subsequent studies, if the treatment period of 3 days is extended, it would be beneficial especially, in monitoring values for kidney functionality closely. Although there are reports of cats and dogs with a history of poisoning after topical applications with products such as thyme oil, no signs of poisoning were observed in any of the 20 dogs in this study. The products used in the summarized literature consisted of a combination of many oils and carrier substances but, in this study, no other substance was used aside from the thyme extract (as revealed by its content analysis) thus, it is thought that the non-toxicity of the thyme extract may be due to the fact that no other active substance was used.

CONCLUSION

In this study, it was concluded that oral use of thyme extract once a day for 3 days is safe for dogs at the concentration and dose used in this study. Considering that the rate of zeroing egg excretion is high in dogs with lower egg numbers in our study, it is predicted that our study will make a significant contribution to research works to be done on thyme extract in different doses or application days in patients with high egg excretion.

ACKNOWLEDGMENTS

Conflict of Interests: The authors declared that there is no conflict of interests.

Financial Disclosure: The authors declared that this study has received no financial support.

Author's Contributions: ÖD, SG, SYD and EK designed the study. SYD and EK did the treatment with Thyme Extract. SG counted parasite eggs in feces. ÖD and EAA did biochemical analyzes. All authors participated in drafting and revising the manuscript. ÖD: Özkan Duru, SG: Sami Gökpınar, SYD: Sibel Yasa Duru, EAA: Elisha Apatewen Akanbong, EK: Erdal Kara. All authors have read and agreed to the published version of the manuscript.

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