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RESEARCH ARTICLE

Influence of the Route of Administration on Therapeutic Efficacy of Ivermectin in Saanen and Damascus Goats Naturally Infected with *Trichostrongylidae* spp.

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Summary

The aims of this study were to compare the therapeutic efficacy of ivermectin after subcutaneous, per os and pour-on administration in Saanen goats naturally infected with *Trichostrongylidea* spp. and to evaluate the efficacy of ivermectin pour-on in Damascus goats with similar gastrointestinal nematodes. After body weighing and faecal sample collection on day 0 (pre-treatment day), 45 Saanen goats were weighed, faecal sampled and allocated on the basis of day -3 faecal egg counts (FEC) to four treatment groups (n=9 in each group). Saanen goats were then treated with a single dose of ivermectin at a dose rate of 0.2 mg/kg by subcutaneous injection or oral administration and 0.5 mg/kg or 1 mg/kg by topical application. Nine Saanen goats were kept as non-medicated control. Fifteen Damascus goats were divided two groups. The first group (n=9) received ivermectin pour-on as a single dose of 0.5 mg/kg and the second group (n=6) served as a non-medicated control. The efficacy was measured on the basis of the reduction of the egg output and the evaluation of the results from larval differentiation on 14 days post-treatment. In Saneen goats, ivermectin provided equally excellent (100%) therapeutic efficacy after subcutaneous or oral administration whereas ivermectin pour-on treatment at a dose of 0.5 mg/kg and 1.0 mg/kg reduced pretreatment FEC by 96.5% and 99.9%, respectively. No statistically significant difference was found between 1.0 mg/kg of ivermectin by topical application and the ivermectin subcutaneous and oral treated groups for post treatment FEC whereas the efficacy of ivermectin pour-on at 0.5 mg/kg was significantly lower than that for each of the other 3 treatment groups. In Damascus goat, the therapeutic efficacy of 0.5 mg/kg ivermectin pour-on was recorded as only 30.7%.

Keywords: *Goat, Saanen, Damascus, Trichostrongylidae, Ivermectin*

Trichostrongylidae spp. ile Doğal Enfekte Saanen ve Damascus (Halep) Keçilerinde İvermektinin Terapötik Etkinliği Üzerine Uygulama Yolunun Etkisi

Özet

Bu çalışmada, *Trichostrongylidea* spp. ile doğal enfekte Saanen keçisinde subkutan, oral ve dökme (pour-on) ivermektin uygulanmasının terapötik etkinliğini karşılaştırılması ve benzer gastrointestinal nematodlarla enfekte Halep keçisinde pour-on ivermektin uygulamasının etkinliğini değerlendirilmesi amaçlanmıştır. Kırk beş Saanen keçisi tedavi öncesi (0. gün) tartılıp, dışkı örnekleri alınmış ve 3 gün öncesi dışkı yumurta sayıları (FEC) temel alınarak 4 tedavi grubuna ayrılmıştır (her grupta n=9). Daha sonra keçilere bir kez 0.2 mg/kg ivermektin subkutan veya oral yolla ve 0.5 mg/kg ya da 1.0 mg/kg topikal olarak uygulanmıştır. Dokuz Saanen keçisi ilaçsız kontrol olarak bırakılmıştır. İki gruba ayrılan 15 Halep keçisinden birinci gruba (n = 9) 0.5 mg/kg tek doz ivermektin pour-on uygulanırken, ikinci grup (n = 6) ilaçsız kontrol olarak tutulmuştur. Etkinlik, tedavi sonrası 14. günde yumurta atılımında azalma ve dışkı kültürü sonuçları baz alınarak değerlendirilmiştir. Saneen keçilerinde subkutan veya oral ivermektin uygulaması eşdeğer tam (%100) terapötik etkinlik sağlarken, 0.5 mg/kg ve 1.0 mg/kg, pour-on ivermektin uygulaması tedavi öncesi dışkı yumurta sayılarını sırasıyla %96.5 ve %99.9 azaltmıştır. Tedavi sonrası FEC açısından 1.0 mg/kg ivermektin pour-on uygulanan grupla, subkutan ve oral ivermektin uygulanan gruplar arasında önemli bir farklılık bulunmazken, 0.5 mg/kg pour-on ivermektin uygulamasının etkinliği, diğer 3 tedavi grubunun her birinden düşük olduğu belirlenmiştir. Halep keçilerinde ise 0.5 mg/kg tek doz ivermektin pour-on uygulamasının etkinliği sadece %30.7 olarak saptanmıştır.

Anahtar sözcükler: *Keçi, Saanen, Damascus, Trichostrongylidae, İvermektin*

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INTRODUCTION

The goat is a high-yield species, which can transform low quality vegetable food into high quality protein sources such as milk and meat. Its husbandry is increasing in importance both in developing countries, mainly as a source of protein, and in developed countries as a product for special markets [1]. Goat husbandry of dairy breeds is increasingly attracting interest as a result of increased demand for goat milk and government support for breeding projects. In this context, the intensive breeding of both the Damascus goat, still raising in Turkey, and the Saanen goat, which could be successfully raised in several regions, has been extending in recent years.

Nematode infections in goats cause important economic losses, directly by the related deaths and indirectly as a result of growth retardation, lost yield, increased sensitivity to other infections and treatment expenses [2,3]. Dairy breed goats are considered to be the most sensitive to nematode infection among domestic animals; this increased sensitivity compared to cattle and sheep is thought to be due to a physiologic character, feeding behavior or natural selection [4]. The progressive increase in intensive breeding of dairy goats in our country is accompanied by an increase in the size of economic losses due to nematode infections. Epidemiological investigation [5-7] showed that, out of 58 helminth species identified in goats in Turkey, five were trematodes, nine cestodes and 44 nematodes, characterizing gastrointestinal nematodes from the *Trichostrongylidae* as the most frequently encountered pathogens in the country as they are worldwide.

Endectocides (avermectins/milbemycin) are among the most important groups of anthelmintic drugs used today to control nematode infections; their use in goats is increasing due to the relatively frequent development of benzimidazole resistance [4]. The frequency of goat nematodes resistant to benzimidazoles is reported to be 70 - 100% in French farms [8,9], while no resistance is mentioned yet to avermectin - milbemycin (endectocide) in contrast to reports from Australia and South Africa. Ivermectin, a *Streptomyces avermitilis* fermentation product, is an avermectin which has been frequently used since its introduction in 1981. The main considerations for the rational use of ivermectin as an anti-nematodal agent are the dose, the route of administration, the yearly treatment schedule, periodicity and the implementation of selective treatment in the animals with severe disease [4,10]. Ivermectin is approved for use in cattle and sheep in many other countries besides Turkey; in goats it is used at the standard dose of 0.2 mg/kg, frequently also recommended for the subcutaneous (SC) treatment of nematode infections of cattle and sheep [4,11-14]. Phamacokinetic studies, however, have shown important differences in ivermectin absorption and elimination as compared to cattle and sheep [4,15,16]. It has therefore been proposed to use a dose of 0.3 mg/kg [1] or 0.4 mg/kg [10] for effective and rational treatment, observing that the use of the cattle or sheep standard dose for nematode infections of the goat may lead to pathogen resistance and impair therapeutic efficacy [4].

Different formulations of ivermectin (injectable, oral and pour-on) are used for nematode infections; the oral and pour-on administration is superior to the SC considering the ease of administration. In the absence of an ivermectin formulation for oral use in the goat, it has been shown that the standard dose for sheep of 0.2 mg/kg is active against goat gastrointestinal nematodes in 90 - 100% of cases, both in experimental [11-13] and natural [14] infections. It was determined that this efficacy of 0.2 mg/kg ivermectin given orally is equivalent to [13] or better than [17-20] that of the same dose administered by SC injection.

Beside the animal species and breed and the strain and biologic phase of the infectious agent, the efficacy rate of ivermectin in the nematode infections of ruminants also varies among different countries and regions, due to the degree of resistance induced by repeated low-dose administration, the frequent repetition of treatment and the time of administration [4,10]. There is, as far as we know, no study in our country comparing the efficacy of SC and oral dosing of ivermectin in Saanen goats naturally infected by *Trichostrongylidae* spp. The activity of the pour-on formulation of ivermectin in gastrointestinal nematode infections, which has been confirmed in several studies performed in cattle [21-23], has not yet been evaluated in goats [4]. The aim of this study was therefore to compare the efficacy of SC *versus* oral ivermectin given at the same dose (0.2 mg/kg) and that of two different doses (0.5 mg/kg *vs* 1 mg/kg) of the pour-on formulation of the same drug in Saanen goats, and to evaluate the efficacy of pour-on ivermectin, 0.5 mg/kg, in Damascus goats.

MATERIAL and METHODS

Animals

This study was planned in the aftermath of the clinical and laboratory evaluation of two Saanen goats, submitted to the Adnan Menderes University Veterinary School Internal Disease Clinic from a farm in the Tire (Izmir) area with growth retardation, diarrhea, weight loss and loss of appetite. It was stated that five other goats in the same farm had died with similar signs, while the others were also sick. An endoparasite infection was suspected on clinical evaluation of these two patients; examination of the feces showed intense infestation by *Trichostrongylidae* spp. A total of 60 female goats breeding on the same farm, 45 of the Saanen and 15 of the Damascus breed, with body weights of 27-55 kg for the former and 30-46 kg for the latter, were thought to be possibly also infected. These two breeds were housed in separate stalls on the farm and the goats have not been grazed on pasture. The animals on the farm had been obtained approximately one year earlier

from different areas of the country (Foça, Izmir for the Saanen and Adana for the Damascus goats) and that they had not been kept together at the same place.

Each of the two breeds of animals was divided into groups according to their count of eggs per gram (EPG) of feces in samples obtained three days before ivermectin treatment (on day 3). Particular attention was paid to dividing the study population, and more particularly the treated animals, in groups with similar EPG counts, while the control groups were comprised of patients with low EPG counts to avoid deaths due to severe *Trichostrongylidae* spp. infection. The Damascus breed included a single treatment group (n=9), because of the small number of total animals, and a control group (n=9), while the Saanen breed animals were divided into five equal groups (n=9 each) of which one was the control group.

Fecal Examination

Fecal samples were collected from each animal by digital rectal examination into individual bags; EPG counts for *Trichostrongylidae* spp. were determined by the McMaster technique [24]. Fecal samples were collected for EPG counts and fecal cultures for identification of parasite strain species, three days prior to treatment (day 3), before the start of treatment on its first day (day 0) and after the end of treatment (day 14). The feces of goats showed the presence of eggs were pooled by groups (two groups each for the Saanen and Damascus breeds); after thorough mixing they were made into a slurry with the addition of water and fine wood shavings (3 parts feces for 1 part wood shavings) to allow for egg development into third stage larvae, collected in plastic containers and incubated one week at 26-28°C [25-28]. During this period, the feces cultures were taken out of the incubator daily for mixing in order to keep them aerated; water was added if the water level was low. The growing larvae were collected by the Baermann-Wetzel method at the end of the incubation time and the larvae diagnosed morphologically according to the related keys [29,30].

Ivermectin Administration

The body weight of each goat was determined by automatic appliances before treatment and drug administration was performed according to individual body weight. The four ivermectin treatment groups into which the Saanen breed goats were divided were as follows: 0.2 mg/kg SC; 0.2 mg/kg orally (O) (both with Baymec® injectable solution 1%, Bayer, Turkey), ivermectin pour-on (Ivomec® pour-on, 0.5% w/v, Merial, Germany) at the standard dose of 0.5 mg/kg (P); finally the same formulation at double the standard dose, i.e. 1 mg kg (Px2), all as a single treatment. The single treatment group in the Damascus breed animals received the pour-on formulation at the dose of 0.5 mg/kg (P) as a single treatment. The control group in either breed was not given any treatment.

The anthelmintic efficacy was determined by the "fecal egg count reduction test" (FECRT) according to the following formula [16].

$$\text{Effect (\%)} = \frac{\text{EPG (pre–treatment)} - \text{EPG (post-treatment)}}{\text{EPG (pre –treatment)}} X100$$

Statistical Evaluation

Statistical evaluation of the data was performed with the SPSS 15.0 software package. The distribution of EPG in both the control and treatment groups on days 0 and 14 was not normal, as indicated by the Kolmogorov-Smirnov test; therefore the comparative statistical evaluation used non-parametric tests. The significance of differences in EPG counts among groups on days 0 and 14 was assessed by the Kruskal-Wallis H test; the Mann-Whitney U test was used to compare the groups and the Wilcoxon test to assess in-group change from day 0 to day 14. The significance limit was defined as a p-value <0.05. Pre and post-treatment (day 0 and 14) EPG counts were expressed as arithmetic mean, standard deviation X±s) and median (interquartile range) *(Table 2)*.

RESULTS

Clinical examination at the first visit to the facility to determine the groups (day 3) and on the first day of treatment (day 0) showed weight loss, irregular hair growth, pallor of mucosas and diarrhea in most animals. The mentioned findings were markedly reduced or had disappeared on day 14 in the treatment groups of the Saanen breed, while the control group animals had no noticeable change in their general condition. The findings were less severe in the Damascus as compared to the Saanen breed goats; most of the clinical findings on day 0 in the latter were still present on day 14. No side effect that could be related to the use or mode of administration of ivermectin was observed in any of the treatment groups in goats of either breed.

Table 1. *Fecal culture results before and after ivermectin treatment*
Tablo 1. *İvermektin tedavisi öncesi ve sonrası dışkı kültürü sonuçları*

Goat Breed	Day 0	%	Day 14	%
Saanen	*Haemonchus contortus*	67		
	Oesophagostomum spp.	19		
	Trichostrongylus spp.	8	*Trichostrongylus* spp.	100
	Cooperia spp.	3		
	Cooperia onchophora	2		
	Ostertagia spp.	1		
Damascus	*Haemonchus contortus*	60	*Haemonchus contortus*	100
	Cooperia onchophora	20		
	Ostertagia spp.	16		
	Cooperia spp.	4		

Table 2. *EPG counts, FECR results and mean EPG change before (day 0) and after treatment (day 14) in Saanen and Damascus breed goats*
Tablo 2. *Saanen ve Damascus keçilerinde oluşturulan gruplarda tedavi öncesi (0. gün) ve tedavi sonrası (14. gün) EPG değerleri, FECR sonuçları ve ortalama EPG değişimleri*

Goat No	Saanen														Damascus				
	SC (0.2 mg/kg) (n=9)			O (0.2 mg/kg) (n=9)			P (0.5 mg/kg) (n=9)			Px2 (1 mg/kg) (n=9)			Control (n=9)		P (0.5 mg/kg) (n=9)			Control (n=6)	
	Day 0	Day 14	FECR %	Day 0	Day 14	FECR %	Day 0	Day 14	FECR %	Day 0	Day 14	FECR %	Day 0	Day 14	Day 0	Day 14	FECR %	Day 0	Day 14
1	21500	0	100	19500	0	100	11350	350	97	10250	0	100	2300	550	3350	2450	27	200	100
2	6450	0	100	7050	0	100	7300	500	93	8750	0	100	1200	450	2850	2800	2	150	100
3	4800	0	100	4900	0	100	5000	50	99	5700	0	100	900	1050	2150	1350	37	50	150
4	4000	0	100	4000	0	100	4400	0	100	4600	0	100	750	2400	1350	1050	22	50	50
5	3000	0	100	3400	0	100	3400	50	99	3600	0	100	300	250	1300	50	96	50	50
6	2650	0	100	2800	0	100	2850	0	100	3000	0	100	200	300	650	1000	-54	50	0
7	1350	0	100	1650	0	100	1650	0	100	1750	50	97	200	1350	550	150	73		
8	950	0	100	950	0	100	1400	350	75	1200	0	100	200	300	500	550	-10		
9	400	0	100	500	0	100	800	50	94	850	0	100	150	150	300	200	33		
X± s	5011.1± 8478.8	**0**		4972.2 ± 5817.3	0		4238.9 ± 3349.7	150.0 ± 193.6		4411.± 3304.1	5.6 ± 16.6		688.9 ± 712.7	755.6 ± 734.6	1483.3 ± 1079.4	1027.8 ± 1003.2		91.7 ± 66.5	75.0 ± 52.4
Median (inter quartile range)	3000 (4475)	**0**[a]		3400 (4675)	**0**[a]		3400 (4625)	**139**[b] (350)		3600 (5750)	**0**[a]		300 (850)	**450**[c] (925)	**1300** (1575)	**650*** (1725)		**50** (112.5)	**75** (75)
	***Mean Effect* %**		**100**	***Mean Effect* %**		**100**	***Mean Effect* %**		**96.5**	***Mean Effect* %**		**99.9**			***Mean Effect* %**		**30.7**		

SC: *subcutaneous administration,* ***O:*** *oral administration,* ***P:*** *pour-on administration,* ***Px2:*** *double dose pour-on administration,* [a,b,c]***:*** *The difference among the day 14 values on the same horizontal line, marked by different letters, is significant,* * *The EPG count pre-treatment (day 0) is significantly different from the one post-treatment on day 14.*

Parasite larvae of the *Trichostrongylidae* found in the feces cultures sampled before treatment in both Saanen and Damascus goats are shown in *Table 1*; *Trichostrongylidae* spp. EPG counts and the statistical evaluation of feces samples of both breeds, pre-treatment on day 0 and after treatment on day 14, are presented in *Table 2*. While six different nematodes were found in the pre-treatment fecal samples of the Saanen and four in the Damascus breed goats, the parasites which were still present in the post-treatment feces of the two breeds were, respectively, *Trichostrongylus* spp. and *Haemonchus contortus (Table 1)*.

Differences among the four different treatment groups in the Saanen goats (SC, O, P and px2) as to EPG counts were not statistically significant (P=0.968), while highly significant differences among groups (P<0.001) appeared on day 14. The median EPG count in this breed was lower than that of the control group in the SC, O and Px2 groups with a p-value <0.001, while the significance level was still P<0.01 in the P group. Median EPG was comparable among the SC, O and Px2 groups (P>0.05), while that of day 14 in the P group remained significantly higher (P<0.01) than in the other three treatment groups. When comparing the pre-treatment day 0 EPG to those on day 14 for the control group and the four treatment groups, the latter all showed an important reduction (P<0.001), while no significant change was seen in the controls. Efficacy, quantified by using the FECR test post-treatment by both SC and oral ivermectin in the Saanen goats naturally infected by *Trichostrongylidae* spp., was 100%; it amounted to 96.5% for the pour-on formulation at a dose of 0.5 mg/kg and 99.9% for double this standard dose by the same route *(Table 2)*.

As for the Damascus breed goats, comparison of the pre-treatment day 0 to day 14 EPG showed a significant decrease in the P group (P<0.01) but no significant change in the control group. Therapeutic efficacy for pour-on treatment with ivermectin, 0.5 mg kg, was determined as being 30.7% according to FECR test results *(Table 2)*.

DISCUSSION

The standard dose of ivermectin administered for different indications in cattle and sheep is 0.2 mg/kg for SC and oral treatment and 0.5 mg/kg for pour-on application. Even though ivermectin has not received registration approval for use in goats, in which its results have been considered suboptimal [1,8,10], it is frequently used in practice by the animal farmers and the veterinarians. This study characterized the efficacy of ivermectin, determined with the help of the FECR test, as being 100% for SC and oral administration at the dose of 0.2 mg/kg, and 96.5% and 99.9%, respectively, for pour-on treatment with 0.5 mg/kg and 1 mg/kg in the Saanen breed goats naturally infected by *Trichostrongylidae* spp. (*Haemonchus contortus, Oesophagostomum* spp., *Trichostrongylus* spp., *Cooperia* spp., *Cooperia onchophora, Ostertagia* spp.); the efficacy of pour-on treatment with ivermectin, 0.5 mg/kg, was 30.7% in the Damascus goat *(Table 2)*.

The antinematode activity of ivermectine varies significantly according to the drug route, dose and formulation, the patient's feeding, physiologic condition and amount of fat tissue, finally the nematode species, biologic phase and resistance status [4]. Compared to oral and pour-on administration, SC injection was shown to be the most efficient route of administration, in goats as well as cattle or sheep, from the bioavailability viewpoint [4,31]. It has been considered that low bioavailability of oral and pour-on administration could be one of the causes of the low efficacy of treatment by these routes [4]. Experimental as well as field studies in goats have shown, however, that oral ivermectin treatment for intestinal nematodes provides an efficacy equivalent to, or better than, that of SC treatment [4,17,18]. The efficacy level of oral ivermectin, 0.2 mg/kg, reported in studies that consider the total parasite load in evaluating treatment efficacy against gastrointestinal nematodes has been reported as being >99% [4,11-13]. In the same context, oral administration of oral ivermectin at the mentioned dose obtained 99.9% efficacy compared to 98.7% for SC administration in goats experimentally infected by *Trichostrongylus colubriformis (T. colibriformis)*. In field studies evaluated by the FECR test, the efficacy of 0.2 mg/kg ivermectin SC in *Trichostrongylus* spp. infection was 94% versus 100% when given orally at the same dose). Borgsteede [32] has shown a difference in efficacy, in experimental infection models in sheep, between SC and oral ivermectin adminis-tration of, respectively, 92% *vs* 100% in *T. vitrinus* and 85.7 *vs* 98% in *Cooperia curticei*. In this study, the efficacy of 0.2 mg/kg SC and oral ivermectin administration was found equivalent in Saanen breed goats naturally infected by *Trichostrongylidae* spp. according to FECR results (100%); this result was compatible with earlier reports showing equivalence of standard dose oral ivermectin with the same dose given SC [4,13]. While it is possible to observe a poorer efficacy of oral ivermectin administration, compared to SC injection, against migrating larvae or tissue forms of nematodes due to lower bioavailability of the oral drug, the oral route can also provide a high gastrointestinal drug concentration, more active against nematodes in the intestinal lumen [16]. While food intake is a negative factor for oral administration, lactation and infectious agent resistance negatively influence both oral and subcutaneous routes [4]. In the Saanen breed goats naturally infected by *Trichostrongylidae* spp. in our study, a 12-hour fast preceding the ivermectin administration, the fact that the animals were not lactating, the absence of previous treatment by a drug of the avermectin group and the optimal individual dosing by body weight measurement for each animal may have contributed to a maximal efficacy (100%) by both routes of administration.

Pour-on drug administration is a preferred method, thanks to its ease of administration necessitating less involvement,

the absence of different sources of possible infective contamination in contrast to parenteral administration, the absence of residual drug at the site of treatment and the possibility of avoiding contact with potentially dangerous animal species. Ivermectin can be applied as a pour-on in addition to SC and oral administration; pour-on ivermectin preparations recommended for administration at a dose of 0.5 mg/kg are available and approved for use in cattle only. The sex-related plasma distribution of ivermectin following pour-on application [33] and the effects of age and dose on ivermectin plasma distribution and hair concentration [34] have been evaluated; no study in the therapeutic efficacy of this route of adminis-tration was hitherto available [4]. Therefore the efficacy of the pour-on administration to Saanen goats naturally infected with *Trichostrongylidae* spp., 96.5% at the recommended standard dose for cattle (0.5 mg/kg) and 99.9% at 1 mg/kg, *(Table 2),* could not be compared to other results. The efficacy of ivermectin at a dose of 0.5 mg/kg (96.5%) was found significantly lower ($P<0.01$) than that of SC and oral administration (100%). The efficacy of pour-on applications of ivermectin for similar purposes in cattle at a dose of 0.5 mg/kg was reported as 80-100% [21-23]. This leads to the idea that bioavailability may be poor following pour-on application of 0.5 mg/kg ivermectin to the Saanen goat.

This study was unable to compare the efficacy of all three routes of administration (SC, oral and pour-on) in the Damascus breed goat because of a small number of animals, insufficient to constitute groups. The efficacy characterized in the Damascus goat infected by *Trichostrongylidae* species similar to those of the Saanen goat was 30.7%, significantly poorer than the 96.5% determined in the latter breed *(Table 2)*. This difference in pour-on administration may have an explanation in anatomical or physiological peculiarities of the breed. In fact, the effect of anatomical and physiological differences of animal species on avermectin pharmacodynamics has been documented [35], as has been the marked difference in iver-mectin plasma levels between Damascus and Kilis goats given the same SC doses [36]. Also, cases of anthelmintic activity falling under 90% by calculation based on the FECR test are characterized as "resistance positive" [37]. The low FECR (30.7%) observed in Damascus goat indicates the presence of gastrointestinal nematodes resistant to ivermectin *(Table 2)*. The faecal cultures examined 14 days after treatment showed that resistance to ivermectin based on the low FECR results from *H. contortus (Table 1),* the most common trichostrongylid of goats in many parts of the World [1-5]. Factors that are of the greatest importance for anthelmintic resistance include generally indiscriminate use and overuse of anthelmintics, a general lack of biosecuriiy on the farm, frequent movement of animals off of and onto the farm, insufficient quarantine procedures for new arrivals, and a failure to treat new arrivals with effective anthelmintics during the quarantine period [1,4]. One or more of these factors may have played a role in resistance to ivermectin in Damascus goat of this study. In particular, frequent and indiscriminate use of ivermectin is commonly practiced by farmers because of its high efficacy, easy application and wide safety indices. As a consequence, there has been an increase in farms reporting the insufficient effect of ivermectin. Damascus goats on the farm in Tire/İzmir have not been previously treated with ivermectin; therefore, resistant *H. concortus* due to possibility of overuse and/or misuse of ivermectin may initially have been bought in with breeding stock from Adana.

In conclusion, it was determined that the administration of either SC or oral ivermectin at the dose of 0.2 mg/kg to Saanen goats naturally infected by *Trichostrongylidae* spp. resulted in full efficacy for both routes, that the efficacy of the pour-on preparation at a dose of 0.5 mg/kg was lower than that of the two other routes of administration, finally that the efficacy when administered by the latter route and dose was very limited in the Damascus goat.

REFERENCES

1. Hoste H, Sotiraki S, Torres-Acosta JFJ: Control of endoparasitic nematode infections in goats. *Vet Clin Food Anim*, 27, 163-173, 2011.

2. Boch J, Supperer R: Nematoden. **In,** Boch J, Supperer R (Hrgb): Veterinaermedizinische Parasitologie. 3. Auflage. 147-201, Verlag Paul Parey, Berlin und Hamburg, 1983.

3. Pawel GR, Niznikowski E, Strzelec D, Popielarczyk A, Gajewska H: Prevalence of protozoan and helminth internal parasite infections in goat and sheep flocks in Poland. *Arch Tierz Dummerstorf*, 47, 43-49, 2004.

4. Lespinea A, Chartierb C, Hostec H, Alvineriea M: Endectocides in goats: Pharmacology, efficacy and use conditions in the context of anthelmintics resistance. *Small Rumınant Res*, 103, 10-17, 2012.

5. Doğanay A, Öge S: Türkiye'de koyun ve keçilerde görülen helmintler. *Kafkas Univ Vet Fak Derg*, 3, 97-114, 1997.

6. Şenlik B, Diker Aİ, Sönmez G, Akyol V: Güney Marmara bölgesindeki kıl keçilerinde nematod türlerinin yayılışı. *Türkiye Parazitol Derg*, 25, 170-173, 2001.

7. Umur Ş, Yukarı BA: Seasonal activity of gastrointestinal nematodes in goats in Burdur region, Turkey. *Turk J Vet Anim Sci*, 29, 441-448, 2005.

8. Chartier C, Soubirac F, Pors I, Silvestre A, Hubert J, Couquet C, Cabaret J: Prevalence of anthelmintic resistance in gastro-intestinal nematodes of dairy goats under extensive management conditions in southwestern France. *J Helminthol,* 75, 325-330, 2001.

9. Paraud C, Pors I, Rehby L, Chartier C: Absence of ivermectin resistance in a survey on dairy goat nematodes in France. *Parasitol Res,* 106, 1475-1479, 2010.

10. Silvestre A, Leignel V, Berrag B, Gasnier N, Humbert JF, Chartiere C, Cabaret J: Sheep and goat nematode resistance to anthelmintics: pro and cons among breeding management factors. *Vet Res,* 33, 465-480, 2002.

11. Swan GE, Gross SJ: Efficacy of ivermectin against induced gastrointestinal nematode infections in goats. *Vet Rec,* 117, 147-149, 1985.

12. McKenna PB, Watson TG: The comparative efficacy of four broad spectrum anthelmintics against some experimentally induced trichostrongylid infections in sheep and goats. *N Z Vet J,* 35, 192-195, 1987.

13. Waruiru RM, Kogi JK, Weda EH, Ngotho JW: Multiple anthelmintic resistance on a goat farm in Kenya. *Vet Parasitol*, 75, 191-197, 1998.

14. Chartier C, Pors I: Efficacy of four broad spectrum anthelmintics against gastrointestinal nematodes in goats. *Vet Rec,* 134, 523-524, 1994.

15. Escudero E, Carceles CM, Diaz MS, Sutra JF, Galtier P, Alvinerie M: Pharmacokinetics of moxidectin and doramectin in goats. *Res Vet Sci,* 67,

177-181, 1999.

16. Gokbulut C, Karademir U, Boyacioglu M: Comparison of plasma pharmacokinetic profile of ivermectin following administration of subcutaneous injection (Baymec) and oral tablet (Efektin) in goats. *J Vet Pharmacol Ther,* 30, 489-491, 2007.

17. Pearson AB, Rutherford DM: Ivermectin injection less effective in goats than oral treatment. *Surveillance*, 15, 22, 1988.

18. McKenna PB: Update on Anthelmintics in Goats. Publication Veterinary Continuing Education, Massey University, pp. 93-96, 1991.

19. Hoyt PG, French DD, Miller JE, Williams JC, Hackett GE, Kearney MT, Hoyt MJ: Evaluation of ivermectin against experimental infections of *Haemonchus contortus* and *Trichostrongylus colubriformis* in goats. *Vet Parasitol,* 42, 257-263, 1992.

20. Rahman WA: Role of ivermectin and its formulations in the control of trichostrongylid nematodes on small holder goat farms of Malaysia. *Small Rumin Res,* 25, 83-87, 1997.

21. Hooke FG, Clement P, Dell'Osa D, Porter RM, MacColl D, Rew RS: Therapeutic and protective efficacy of doramectin injectable against gastro-intestinal nematodes in cattle in New Zealand: a comparison with moxidectin and ivermectin pour-on formulations. *Vet Parasitol,* 72, 43-51, 1997.

22. Islam IM, Mostofa M, Rofiq K: Efficacy of ivermectin (pour on formulation) against gastrointestinal nematodiasis in cattle of Bangladesh. *Indian J Pharmacol,* 31, 234-236, 1999.

23. Ballweber LR, Smith LL, Stuedemann JA, Yazwinski TA, Skogerboe TL: The effectiveness of a single treatment with doramectin or ivermectin in the control of gastrointestinalnematodes in grazing yearling stocker cattle. *Vet Parasitol,* 72, 53-68, 1997.

24. MAFF: Manual of Veterinary Parasitological Laboratory Techniques Reference Book Vol. 418. 3th ed., pp. 159, Ministry of Agriculture, HMSO, London, 1986.

25. Sangster NC: Pharmacology of anthelmintic resistance in cyathostomes: Will it occur with the avermectin/milbemycins? *Vet Parasitol,* 85, 189-201, 1999.

26. Soulsby EJL: Textbook of Veterinary Clinical Parasitology, Volume 1. 797-805, Blackwell Scientific Publication, Oxford, 1965.

27. Stoye M: Parasitologische Laboruntersuchungen in der Praxis. *Prakt Tierarzt,* 65, 132-136, 1984.

28. Thienpont D, Rochette F, Vanparijs OFL: Diagnosing Helminthiasis by Coprological Examination. 2th ed., p. 187, Janssen Research Foundaton, Belgium, 1986.

29. Van Wyk JA, Cabaret J, Michael LM: Morphological identification of nematode larvae of small ruminants and cattle simplified. *Vet Parasitol*, 119, 277-306, 2004.

30. Şenlik B: Teşhis Yöntemleri. **In,** Tınar R (Ed): Helmintoloji. s. 463-535, Nobel Yayın Dağıtım, Ankara, 2006.

31. Alvinerie M: Comparative pharmacokinetic properties of moxidectin and ivermectin in different animal species. *J Vet Pharmacol Ther,* 20, 74, 1997.

32. Borgsteede FH: The efficacy and persistent anthelmintic effect of ivermectin in sheep. *Vet Parasitol,* 50, 117-124, 1993.

33. Gokbulut C, Bilgili A, Hanedan B, Aksit D, Aksoy AM, Turgut C: Sex-related plasma disposition of ivermectin following pouron administration in goats. *Vet Parasitol*, 162, 342-345, 2009.

34. Gokbulut C, Cirak VY, Senlik B, Aksit D, McKellar QA: The effects of different ages and dosages on the plasma disposition and hair concentration profile of ivermectin following pour-on administration in goats. *J Vet Pharmacol Ther,* 34, 70-75, 2011.

35. McKellar QA, Gokbulut C: Pharmacokinetic features of the antiparasitic macrocyclic lactones. *Curr Pharm Biotechnol*, 13, 888-911, 2012.

36. Gokbulut C, Bilgili A, Hanedan B, Aksit D, Aksoy AM, Turgut C: Breed-related plasma disposition of ivermectin following subcutaneous administration in Kilis and Damascus goats. *Res Vet Sci*, 87, 445-448, 2009.

37. Coles GC, Bauer C, Borgsteede FH, Geerts S, Klei TR, Taylor MA, Waller PJ: World Association for the Advancement of Veterinary Parasitology (WAAVP) methods for the detection of anthelmintic resistance in nematodes of veterinary importance. *Vet Parasitol,* 44, 35-44, 1992.