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## HAEMATOLOGICAL RESPONSE IN THE TREATMENT OF NATURALLY ACQUIRED ECTOPARASITE INFESTATIONS IN RABBITS

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**Abstract:** The objective of this study was to determine changes in haematological values of topical administration of selamectin in rabbits with at least one species of naturally acquired ectoparasite infestation (*Sarcoptes scabiei* var. *cuniculi*, *Psoroptes cuniculi*, or *Cheyletiella* spp). Thirty-five rabbits were enrolled. They underwent physical examination and assessment of ectoparasite infestations on days 0, 14, 28, 56 and 86. Blood for haematology and serum biochemistry was collected on days 0, 14, 28 and 56. Selamectin was topically applied at a dose of 15 mg/kg onto the skin on days 0, 14 and 28, respectively. No ectoparasites or eggs were found in these rabbits from day 28 onwards by skin scraping and/or tape cytology. Haematology and serum biochemistry values were within normal limit throughout the study. However, the neutrophil to lymphocyte ratio significantly decreased post-treatment from 2.89 (0.90-5.47) on day 0 to 1.38 (0.56-3.09), and 1.44 (0.42-4.47) on days 14 and 56, respectively. There were no adverse drug reactions or treatment-related mortalities during the study. This study indicated that selamectin was effective and safe in the treatment and prevent re-infestation for at least 58 d post-treatment. Moreover, the neutrophil to lymphocyte ratio could be used for monitoring of inflammatory response in rabbits.

**Key Words:** ectoparasite, haematology, lymphocyte, neutrophil, rabbit, selamectin.

## INTRODUCTION

Rabbits have not only been used as pets or laboratory animals, but also for meat production. Most commercial rabbit farms in Thailand are small in size, where appropriate wellness care programmes and farm management are neglected. Control of ectoparasite infestations in rabbits has been overlooked, which leads to reduction in production and increase husbandry costs (Mikled *et al.*, 2008). To date, reports on the prevalence of ectoparasites in rabbits in Thailand and Southeast Asia are limited. However, anecdotal findings of ectoparasites in veterinary practices included *Psoroptes cuniculi*, *Sarcoptes scabiei* var. *cuniculi*, and *Cheyletiella parasitovorax*.

Selamectin (Revolution<sup>®</sup>, Zoetis Inc., Kalamazoo, MI, USA), a macrocyclic lactone of the avermectin compound, is available as a spot-on formulation. It is a safe, broad-spectrum parasiticide approved for topical use in dogs and cats. However, selamectin is not licensed for treating ectoparasites in rabbits (Fisher *et al.*, 2007). The extra-label use of selamectin for the treatment of ectoparasites and endoparasites in rabbits has been reviewed and suggested (Fisher

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*et al.*, 2007), including *Psoroptes cuniculi* at a dose of 6 or 18 mg/kg, given once or twice with an interval of 28 d between treatments (McTier *et al.*, 2003), or at doses of 6 to 18 mg/kg in one application (Kurtdebe *et al.*, 2007); *Sarcoptes scabiei* var. *cuniculi* at doses of 8 to 14 mg/kg twice, 30 d apart (Farmaki *et al.*, 2009) or at doses of 8 to 14 mg/kg once (Kurtdebe *et al.*, 2007); and *Cheyletiella* spp. at a dose of 12 mg/kg once (Kim *et al.*, 2008) or at doses of 6.2-20.0 mg/kg, 1-3 times with an interval of 2-4 wk (Mellgren and Bergvall, 2008). Selamectin at a dose of 20 mg/kg given every week for 3 wk was efficient for the treatment of flea infestation in rabbits, with no adverse reaction (Carpenter *et al.*, 2012).

Data on haematological and serum biochemical parameters in healthy rabbits and rabbits with clinical diseases have increased, together with the increasing popularity of rabbits as pets (Hinton *et al.*, 1982; Archetti *et al.*, 2008; Özkan *et al.*, 2012), but also in rabbit farmed for meat production (Belhassen *et al.*, 2016; Stancu *et al.*, 2017; Sun *et al.*, 2018). The aim of the study was to investigate changes in haematology and selected biochemistry in the use of topical administration of selamectin for the treatment of naturally acquired ectoparasite infestations in farm rabbits.

## MATERIALS AND METHODS

### **Animal care**

The protocol used in the present study was approved by the Faculty of Veterinary Science Animal Care and Use Committee, no. MUVS-2015-18, Mahidol University, Thailand. This was a prospective, non-controlled study carried out from June to September 2015.

### **Animals, farm and management**

To be eligible for inclusion, a rabbit had to be older than 2 mo, had at least one of these ectoparasite infestations (*Psoroptes cuniculi*, *Sarcoptes scabiei* var. *cuniculi*, and *Cheyletiella* spp), and had not been treated with ectoparasiticides, antibiotics, steroidal anti-inflammatory drugs, or non-steroidal anti-inflammatory drugs, in the last 90 d before the study. Rabbits were excluded from the study if they were pregnant or suffering from severe systemic illness. Power calculations for study population size were performed by G\*Power version 3.1.7 (Heinrich-Heine-Universität Düsseldorf, <http://www.gpower.hhu.de>). For the power analysis on a repeated measures ANOVA with 4 measurements, a power of 0.80, an alpha level of 0.05, and a medium effect size ( $f=0.25$ ) (Faul *et al.*, 2013), the required sample size was 24.

Thirty-five rabbits recruited into this study were obtained from a commercial rabbit farm in the rural area of Karnchanaburi province, the western region of Thailand. There were 13 males and 22 females, mixed breed, the average±standard deviation (SD) of age was 15.57±5.42 mo (ranged from 5 to 24 mo), and the average±SD of body weight in the first assessment on day 0 (pre-treatment) was 2.54±0.60 kg (ranged from 1.16 to 3.6 kg). These rabbits were housed in wire cages individually with natural atmosphere and ventilation. They were given *ad libitum* access to commercial diet of approximately 14-16% protein and water.

Rabbits underwent physical examination from head to tail, starting from observation of their attitude, mental alertness, skin and hair coat, respiration, and posture. Hydration status was evaluated by skin tent and capillary refill time (CRT). Mucous membrane was assessed by examination of the conjunctiva or oral cavity. Palpation of the thoracic cage, abdomen, and extremities was carried out. Auscultation of the heart and lungs was also performed. All rabbits underwent physical examination and their body weight was weighed in the same way on days 0, 14, 28, 56 and 86.

### **Assessment of ectoparasite infestations**

The rabbits enrolled in the present study had at least one ectoparasite infestation assessed by detection of live mites from both skin scrapings and tape cytology between 4 to 8 sites. Skin scrapings and tape cytology were taken from each rabbit from sites showing the most likelihood for ectoparasite infestation; for example, ear margins, feet, and pruritic and/or lesioned skin (any crusts, scales, papules, erythema, and alopecia). Each skin scraping or tape cytology was carried out over an area of about one square inch. Skin scraping was performed to an approximately constant depth, following one or two drops of mineral oil placed on the skin. The material obtained was transferred to

mineral oil on microscope slides. These slides and tape cytology were examined by microscopic examination under low power magnification ( $\times 4$  or  $\times 10$ ).

The severity of the clinical manifestations of affected areas were classified to be “absent” if no abnormality detected; “mild” if the intensity of the manifestation was low and only a small area of the body was affected; “moderate” if the manifestation was great intensity over a small area or a lower intensity over a large area of the body; and “severe” if the manifestation was great intensity over a large area of the body. Affected areas of the body were recorded as ear (including head and neck), body (thorax and abdomen) and extremities.

### ***Blood collections and evaluations***

A total of 2 mL of blood was collected from the lateral saphenous vein of each rabbit into tripotassium ethylenediaminetetraacetic acid (K3-EDTA)-treated and plain tubes to evaluate haematology and selected serum biochemistry parameters (alanine aminotransferase [ALT], aspartate aminotransferase [AST], blood urea nitrogen [BUN], and creatinine) on days 0, 14, 28 and 56. All blood samples were collected in the afternoon between 12:00 pm to 6:00 pm. A 24-gauge sterile needle was used in every rabbit. Serum was separated from blood within 30 min of collection. Blood in K3-EDTA-treated and serum samples were transported to the laboratory at 4°C within 18 h for haematological and biochemical analyses. Haematological parameters were evaluated by Animal Blood Counter ABC™ (Horiba ABX Diagnostic (Thailand) Ltd., Bangkok, Thailand). Recommended settings and calibration for rabbit haematology were applied according to the manufacturer’s protocol. Serum biochemistry parameters were assessed by a Sapphire 400 Auto-Chemistry Analyzer (D.A.P. Siam Group Ltd, Bangkok, Thailand) using kits by the same company. The parameters and the respective methods employed are as follows: ALT/AST—kinetic 37°C/kinetic without pyridoxal method, BUN—enzyme kinetic method, and creatinine—Jaffe kinetic method.

### ***Treatment***

Selamectin (Revolution® Green for dogs, each tube containing 2 mL of 12% selamectin (120 mg/mL), Zoetis Inc, Kalamazoo, MI, USA) was topically applied onto the skin at the base of the neck at a dose of 15 mg/kg body weight following physical examination, skin scrapings, tape cytology and blood collection. Repeated treatments were performed in the same manner on days 14 and 28 in order to kill all adults of *Psoroptes cuniculi*, *Sarcoptes scabiei* var. *cuniculi*, and *Cheyletiella parasitovorax* and to prevent re-infestation from egg to adult of these ectoparasites.

### ***Statistical analysis***

Computerised statistical software (SPSS 18.0 for Windows, Chicago, IL, USA) was used for analyses. Probabilities  $< 0.05$  were considered statistical significant. The numerical parameters obtained from each day of examination were tested for normality by the Shapiro-Wilk test. Comparisons of numerical variables on days 0, 14, 28, 56 and 86 were performed within rabbits by repeated measure ANOVA with a Bonferroni comparison for post-hoc analyses. The Friedman test was carried out to compare the severity of the clinical manifestations of each affected area within the subjects on days 0, 14, 28, 56 and 86.

## **RESULTS**

Distribution of number of rabbits with ectoparasite infestations and percentage of parasitological cure rate obtained from day 0, 14, 28, 56 and 86 are illustrated in Table 1. There were no adverse drug reactions or treatment-related mortalities during the study. Ectoparasites were still found in three rabbits on day 14 with either of *Psoroptes cuniculi*, *Sarcoptes scabiei* var. *cuniculi*, or both *Sarcoptes scabiei* var. *cuniculi* and *Cheyletiella* spp. No ectoparasites or eggs were found from skin scrapings or tape cytology in all rabbits from day 28 onwards. No evidence of recurrent infestation on day 58 following the third treatment on day 28 was observed.

The severity of the clinical manifestations of affected areas was significantly decreased with time (Table 2, all  $P < 0.01$ ). Friedman test was used to compared the severity of the clinical manifestations within the subjects on days 0, 14, 28, 56 and 86. There were significantly different obtained from all areas between day 0 and day 14, day 0 and day 28,

**Table 1:** Efficacy of selamectin against natural infestation of ectoparasites in 35 rabbits.

Type of infestations	Number of rabbits with ectoparasite infestations and (%) of parasitological cure rate				
	Day 0	Day 14	Day 28	Day 56	Day 86
<i>Psoroptes cuniculi</i>	1 (0)	1 (0)	0 (100)	0 (100)	0 (100)
<i>Sarcoptes scabiei</i> var. <i>cuniculi</i>	16 (0)	1 (93.75)	0 (100)	0 (100)	0 (100)
<i>Cheyletiella</i> spp.	1 (0)	0 (100)	0 (100)	0 (100)	0 (100)
<i>Psoroptes cuniculi</i> & <i>Cheyletiella</i> spp.	1 (0)	0 (100)	0 (100)	0 (100)	0 (100)
<i>Sarcoptes scabiei</i> var. <i>cuniculi</i> & <i>Cheyletiella</i> spp.	16 (0)	1 (93.75)	0 (100)	0 (100)	0 (100)

Selamectin 15 mg/kg was administered topically in a single spot following physical examination, skin scrapings and tape cytology on day 0, 14 and 28, respectively. Results display numbers of rabbits with ectoparasites present and percentages (in brackets) of parasitological cure rate obtained from days 0, 14, 28, 56 and 86, respectively.

day 0 and day 56, day 0 and day 86, day 14 and day 28, day 14 and day 56 and day 14 and day 86 (all  $P < 0.01$ ). No differences were obtained from any areas between day 28 and 56, day 28 and 86, and day 56 and day 86 ( $P > 0.05$ ).

Haematological values and serum biochemistry values; ALT, AST, BUN and creatinine on days 0, 14, 28 and 56 are shown in Table 3. Haematological parameters obtained from day 0, 14, 28 and 56 were in accordance with those of healthy rabbits in previous studies (Hinton *et al.*, 1982; Archetti *et al.*, 2008; Özkan *et al.*, 2012). However, the total white blood cell (WBC) count measured on day 0 was higher than on day 28 ( $P = 0.005$ ). Neutrophils, monocytes, and neutrophil/lymphocyte ratio were higher on day 0 when compared to days 14 ( $P < 0.01$ ), 28 ( $P = 0.03$ ) and 56 ( $P < 0.01$ ), whereas lymphocytes, erythrocytes, haemoglobin, and packed cell volume (PCV) were lower on day 0. The AST, BUN and creatinine values in the present study overlapped those reported by other authors in healthy rabbits (Özkan *et al.*, 2012; Varga, 2014). However, serum ALT levels obtained from 25% of these rabbits were higher than those reported by Özkan *et al.* (2012) and Varga (2014). Interestingly, BUN was lower on day 56 when compared to days 0 ( $P = 0.002$ ), 14 ( $P = 0.04$ ) and 28 ( $P = 0.001$ ) respectively, which was similar to the changes in creatinine levels.

The body weight of the rabbits was significantly increased with time during the study ( $P < 0.01$ , Figure 1). Mean  $\pm$  SD of the body weight of the rabbits on days 0, 14, 28, 56 and 86 were 2.54  $\pm$  0.60 kg, 2.72  $\pm$  0.62 kg, 2.87  $\pm$  0.56 kg, 3.01  $\pm$  0.53 kg, and 3.13  $\pm$  0.53 kg, respectively.

**Table 2:** Severity of the clinical manifestations, number of rabbits and percentages (in brackets), on days 0, 14, 28, 56 and 86.

Affected area	Day 0	Day 14	Day 28	Day 56	Day 86	P
Ear (including head and neck)						<0.01
Absent	3 (8.6)	14 (40.0)	35 (100.0)	35 (100.0)	35 (100.0)	
Mild	11 (31.4)	18 (51.4)	0 (0)	0 (0)	0 (0)	
Moderate	8 (22.9)	2 (5.7)	0 (0)	0 (0)	0 (0)	
Severe	13 (37.1)	1 (2.9)	0 (0)	0 (0)	0 (0)	
Body (thorax and abdomen)						<0.01
Absent	9 (25.7)	23 (65.7)	35 (100.0)	35 (100.0)	35 (100.0)	
Mild	22 (62.9)	12 (34.3)	0 (0)	0 (0)	0 (0)	
Moderate	2 (5.7)	0 (0)	0 (0)	0 (0)	0 (0)	
Severe	2 (5.7)	0 (0)	0 (0)	0 (0)	0 (0)	
Extremities						<0.01
Absent	1 (2.9)	18 (51.4)	34 (97.1)	35 (100.0)	35 (100.0)	
Mild	19 (54.3)	16 (45.7)	1 (2.9)	0 (0)	0 (0)	
Moderate	6 (17.1)	1 (2.9)	0 (0)	0 (0)	0 (0)	
Severe	9 (25.7)	0 (0)	0 (0)	0 (0)	0 (0)	

The severity of the clinical manifestations of affected areas were classified as absent, mild, moderate, and severe on days 0, 14, 28, 56 and 86.

Table 3: Haematological parameters, ALT, AST, BUN, and creatinine obtained from day 0, 14, 28 and 56.

Parameters	Day 0	Day 14	Day 28	Day 56	P (model)	P (post-hoc)
Erythrocytes (10 <sup>12</sup> /L)	6.09 <sup>a</sup> (4.77-7.25)	7.00 <sup>b</sup> (5.60-8.30)	6.26 <sup>a</sup> (5.09-7.76)	6.90 <sup>b</sup> (5.54-8.37)	<0.01	<sup>a=b=c=d</sup> <0.01
Haemoglobin (g/dL)	12.0 <sup>a</sup> (8.8-14.7)	12.8 <sup>b</sup> (10.5-15.0)	12.6 <sup>b</sup> (9.6-15.5)	14.1 <sup>c</sup> (11.1-16.7)	<0.01	<sup>a</sup> 0.01, <sup>b</sup> 0.04, <sup>c=d</sup> <0.01
PCV (%)	37 <sup>a</sup> (28-44)	43 <sup>b</sup> (35-50)	39 <sup>b</sup> (30-47)	43 <sup>b</sup> (35-51)	<0.01	<sup>a=b=c=d</sup> <0.01
MCV (fL)	61 (54-65)	62 (54-68)	62 (53-70)	62 (53-67)	0.06	
MCH (pg)	19.8 <sup>b</sup> (16.2-22.1)	18.2 <sup>a</sup> (15.6-20.7)	20.2 <sup>bc</sup> (16.7-22.8)	20.5 <sup>c</sup> (16.8-22.9)	<0.01	<sup>a=b=c=d</sup> <0.01
MCHC (g/dL)	32.5 <sup>b</sup> (29.9-34.1)	29.6 <sup>a</sup> (28.0-31.0)	32.6 <sup>bc</sup> (31.4-33.6)	33.0 <sup>c</sup> (31.6-34.4)	<0.01	<sup>a=b=c=d</sup> <0.01, <sup>b</sup> 0.04
Platelets (10 <sup>9</sup> /L)	484 <sup>b</sup> (160-887)	463 <sup>ab</sup> (199-920)	396 <sup>a</sup> (159-680)	411 <sup>ab</sup> (212-662)	0.005	<sup>a</sup> 0.01
WBC (10 <sup>9</sup> /L)	7.4 <sup>b</sup> (3.5-12.6)	7.0 <sup>ab</sup> (4.0-13.5)	6.2 <sup>a</sup> (3.5-12.4)	7.0 <sup>ab</sup> (3.6-13.0)	0.008	<sup>a</sup> 0.005
Neutrophils (10 <sup>9</sup> /L)	5070 <sup>b</sup> (2065-9828)	3770 <sup>a</sup> (1628-7560)	3823 <sup>ab</sup> (1064-9424)	3770 <sup>a</sup> (1568-8060)	0.02	<sup>a=b</sup> 0.04
Lymphocytes (10 <sup>6</sup> /L)	1960 <sup>b</sup> (1007-3999)	2882 <sup>b</sup> (1300-4860)	2270 <sup>a</sup> (462-4736)	2954 <sup>c</sup> (1440-5200)	<0.01	<sup>a,b</sup> <0.01, <sup>c</sup> 0.006, <sup>d</sup> 0.001
Monocytes (10 <sup>6</sup> /L)	354 <sup>b</sup> (60-1443)	320 <sup>b</sup> (65-1080)	137 <sup>a</sup> (36-528)	212 <sup>a</sup> (49-632)	<0.01	<sup>a</sup> <0.01, <sup>b</sup> 0.03, <sup>c</sup> 0.001
Eosinophils (10 <sup>6</sup> /L)	22 (0-204)	8 (0-85)	16 (0-189)	25 (0-154)	0.31	
Basophils (10 <sup>6</sup> /L)	0	0	0	2.2 (0-77)	0.38	
Band neutrophils (10 <sup>9</sup> /L)	0	0	0.06 (0-1)	0	0.11	
Neutrophil/lymphocyte ratio	2.89 <sup>b</sup> (0.90-5.47)	1.38 <sup>a</sup> (0.56-3.09)	2.03 <sup>b</sup> (0.40-12.14)	1.44 <sup>a</sup> (0.42-4.47)	<0.01	<sup>a</sup> <0.01, <sup>b</sup> 0.03, <sup>c</sup> <0.01
ALT (IU/L)	60 (8-113)	70 (33-129)	63 (28-208)	69 (21-209)	0.37	
AST (IU/L)	26 (3-100)	32 (8-128)	21 (8-53)	14 (5-192)	0.23	
BUN (mg/dL)	17 <sup>b</sup> (11-30)	16 <sup>b</sup> (10-20)	17 <sup>b</sup> (10-32)	14 <sup>a</sup> (7-21)	<0.01	<sup>a</sup> 0.002, <sup>b</sup> 0.04, <sup>c</sup> 0.001
Creatinine (mg/dL)	1.2 <sup>c</sup> (0.3-1.7)	1.2 <sup>c</sup> (0.7-1.5)	1.0 <sup>b</sup> (0.7-1.3)	1.0 <sup>b</sup> (0.7-1.4)	<0.01	<sup>a=c</sup> <0.01, <sup>b</sup> 0.001

Results are illustrated in mean (minimum-maximum). Statistical differences between day 0, 14, 28 and 56 were tested by repeated measure ANOVA with a Bonferroni comparison for post-hoc analyses. Means in a row not sharing the same letter were significantly different at P<0.05.

PCV, packed cell volume; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; WBC, total white blood cell count; ALT, alanine aminotransferase; AST, aspartate aminotransferase, BUN, blood urea nitrogen.

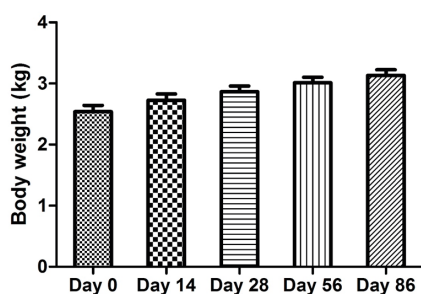


Figure 1: Average of body weight of the rabbits.

## DISCUSSION

Assessment of efficacy of selamectin in the present study was based on ectoparasites detected by skin scrapings and tape cytology and its safety was evaluated from general examination, evidence of adverse reaction, haematological values, and selected parameters of serum biochemistry. The present study showed that 100% of the rabbits in our sample with natural ectoparasite infestations were cured after 2 consecutive treatments of selamectin topical application on day 0 and day 14, whereas one topical application was effective to cure 91.4%. The life cycles from egg to adult of *Sarcoptes scabiei* var. *cuniculi*, *Psoroptes cuniculi* and *Cheyletiella* spp. are completed within 2-3 wk, 3 and 5 wk, respectively (Wall and Shearer,

2001). As the course of this study was extended to 58 d after the last topical application, this would allow the mite numbers to increase based on their life cycle from egg to adult. This study also suggested that three consecutive applications of selamectin at dose of 15 mg/kg body weight every 2 wk could prevent re-infestation by ectoparasites in rabbits for at least 58 d after the last application. Selamectin has been shown to be effective and safe against ectoparasites in rabbits as well as in dogs and cats (Shanks *et al.*, 2000; Six *et al.*, 2000; McTier *et al.*, 2003; Curtis, 2004; Kurtdede *et al.*, 2007). To date, there has been no report of adverse reaction or toxicity regarding the usage of a single spot-on of selamectin in rabbits (McTier *et al.*, 2003; Kurtdede *et al.*, 2007; Carpenter *et al.*, 2012). We also found no adverse reactions associated with selamectin in the present study following each episode of 3 consecutive doses of 15 mg/kg body weight.

This was the first study reporting changes in haematological parameters in the use of selamectin for the treatment of naturally acquired ectoparasite infestations in rabbits. The post-treatment haematological findings were significantly different from pre-treatment, including the increase in erythrocytes, PCV, haemoglobin, and lymphocytes, and the decrease in the total WBC count, neutrophils and monocytes. Reference ranges of normal haematological parameters reported from previous studies have varied (Etim *et al.*, 2014). We therefore interpreted haematological parameters with reference to these reports (Hinton *et al.*, 1982; Bortolotti *et al.*, 1989; Archetti *et al.*, 2008; Özkan *et al.*, 2012; Varga, 2014; Cray, 2015; Moore *et al.*, 2015) in conjunction with the normal hydration status obtained from physical examination. The total WBC count pre- and post- treatments from most of the rabbits in the present study was within normal reference range (Hinton *et al.*, 1982; Bortolotti *et al.*, 1989; Archetti *et al.*, 2008), but it was significantly lower on day 28 when compared to pre-treatment. Leucocytosis is uncommon in rabbits, even in the presence of inflammation or infection (Toth and Krueger, 1988; Toth and January, 1990; Harcourt-Brown and Baker, 2001). These reports were in agreement with the present study, where total WBC count was not increased even in the pre-treatment rabbits. However, the neutrophil to lymphocyte ratio significantly decreased post-treatment, with nearly 1:1 on day 56 of the study. Monocyte counts obtained from every examination were within the normal limit of 2-10% of total WBC (Varga, 2014), but they decreased significantly post-treatment. This may suggest that chronic inflammation affected these rabbits before treatment. Interestingly, eosinophils did not change over the period of the study and values were within the normal limit of 0-5% for total WBC. Eosinophilia is linked to parasitic disease in other species (Melillo, 2007; Varga, 2014), but not in this study. Taken together, we would suggest that the neutrophil to lymphocyte ratio is the most predictive value for the inflammation response and ectoparasite infestations in rabbits. It was reported that the normal ratio of neutrophils to lymphocytes in rabbit over one year of age was approximately 1:1 (Varga, 2014). Stress and diseases can influence this ratio, as it was a method suggested to predict health of rabbits and can be applied to predict diseased status in these rabbits.

The published normal reference ranges for PCV varies between studies, with values between 30% to 50% (Hinton *et al.*, 1982; Melillo, 2007; Archetti *et al.*, 2008; Marshall, 2008; Özkan *et al.*, 2012; Cray, 2015; Moore *et al.*, 2015), but pet rabbits frequently have lower PCV of 30% to 40% (Harcourt-Brown and Baker, 2001). Before treatment, approximately 25% of rabbits in the present study had PCV less than 30% together with lower RBC and haemoglobin

levels, which may suggest that these rabbits had regenerative anaemia due to ectoparasite infestations, as these parameters increased significantly post-treatment.

Serum biochemistry parameter; AST, BUN and creatinine were within the normal range (Melillo, 2007; Archetti *et al.*, 2008; Özkan *et al.*, 2012) throughout the study, although BUN and creatinine measured on day 56 were lower than on days 0, 14 and 28. Moreover, ALT was higher than the normal range in a quarter of these rabbits. This would be a normal result, as slightly increased ALT levels are a common finding in healthy rabbits (Marshall, 2008; Varga, 2014). Taken together, this study suggested that ectoparasite infestations and selamectin treatment did not affect liver or renal function of rabbits.

The present study also demonstrated that ectoparasite infestations in rabbits affected their quality of life. The body weight noticeably increased after the treatments. Taken together with improvement of skin lesions and haematological changes, it indicated that the rabbits were free to consume *ad libitum* diet when their illness had gradually resolved.

This study has several limitations. First, we conducted the study in only one commercial rabbit farm where we were requested to provide a veterinary service. However, this farm was isolated from other farms and rabbits were reared in the same environment, with good ventilation and welfare. This study appeared more similar to experimental conditions rather than a field study. Second, this study was conducted in a prospective, non-controlled fashion which provided limited evidence to compare treatment and placebo. Third, we evaluated hydration status from physical examination and did not find dehydration in these rabbits. Therefore, we assumed that the haematological and serum biochemistry values obtained in this study were measured from rabbits with normal hydration status.

## CONCLUSIONS

In this field study, topical selamectin application of 15 mg/kg at two-week interval was completely effective in the treatment of naturally acquired infestations of *Sarcoptes scabiei* var. *cuniculi*, *Psoroptes cuniculi* and *Cheyletiella* spp. in rabbits. One more dose of 15 mg/kg application on day 28 proved to be effective in the treatment and prevent re-infestation for at least 58 d post-treatment. This study has shown selamectin to be safe for field use in rabbits. Moreover, the neutrophil to lymphocyte ratio can be used for monitoring of inflammatory response in rabbits.

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