Short Communication

Efficacy of 10% w/v fipronil spot-on against tick (*Rhipicephalus sanguineus*) infestation on Cats

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Abstract

The efficacy of 10% w/v fipronil spot-on for treatment and prevention of *Rhipicephalus sanguineus* infestation on cats was examined. Twelve cats were randomly allocated into two groups which were the treatment and control groups. The treatment group received 10% fipronil spot-on at a dosage of 6.7 mg/kg on day 0. A group of 60 *R. sanguineus* was released to feed on each cat on days -7, -2, 3, 7, 14, 21, and 28. The ticks were counted and removed on days -4, 3, 6, 10, 17, 24, and 31. The infested ticks on the cats were also counted but not removed on day 0. Geometric mean number of tick infestation in the control group ranged from 20.83 to 26.17 ticks per cat, or the attachment rate of 34.72 to 43.62% and the mean attachment rate of 39.41%. Geometric mean number of tick infestation in the treatment group on the days before fipronil was applied on the cats ranged from 24.50 to 25.83 ticks per cat, or the attachment rate of 40.83 to 43.06% and the mean attachment rate of 41.95%. Percentages of the efficacy of fipronil used in this study were 99.24, 100, 100, 100, 99.18 and 99.24% on days 3, 6, 10, 17, 24, and 31, respectively. There were statistically significant differences between the geometric mean numbers of tick infestation between the control and treatment groups on days 3, 6, 10, 17, 24, and 31.

Keywords: feline efficacy, fipronil spot-on, *Rhipicephalus sanguineus*, cat

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Introduction

Ectoparasite infestation is one of the most important life threat to cat health worldwide (Chomel et al., 1996; Slapeta et al., 2011; Wedincamp and Foil, 2002). Ectoparasite causes anemia and also plays an important role as a vector of many pathogens in cats (Mendes-de-Almeida et al., 2011). Ectoparasite infestation in cats also plays a crucial role in disease transmission from cats to humans (Shaw et al., 2004). Ectoparasites from cats cause intensive allergic reaction in humans with symptoms of itch, severe irritation, and skin infection (Youssefi et al., 2014; Youssefi and Rahimi, 2014). There are various ectoparasites found on cats including flea, louse, mite, and tick (Changbunjong et al., 2011; Jeffery et al., 2012; Slapeta et al., 2011). Tick infestation on cats in Thailand can be found occasionally, particularly in areas that are infested with a high number of ticks. *Rhipicephalus sanguineus* or brown dog tick is the species that is normally found on dogs in Thailand. Sometimes it is found on cats in urban areas with high population of dogs and cats in Thailand. *R. sanguineus* infestation is also found on cats in Rio de Janeiro, Brazil (Mendes-de-Almeida et al., 2011).

The study by Claerebout et al. (2013) indicated that collected ticks found on cats in Belgium were *Ixodes ricinus* and *I. hexagonus* and most ticks were recovered from head and neck. Ogden et al. (2000) found that tick infestation on cats in Great Britain and Ireland were *I. ricinus*, *I. hexagonus*, and *I. canisuga*.

Haemaphysalis longicornis is the species of most ticks found on cats in Japan, followed by *I. ovatus*, *I. nipponensis*, and *H. flava*. Small numbers of *H. megaspinosa*, *H. japonica*, *I. persulcatus*, *I. granulatus*, and *Amblyomma testudinarium* were also recovered on cats in Japan. *H. longicornis* is frequently found on cats around riversides or river basins, while *I. ovatus* and *I. nipponensis* are more frequently found on cats kept near woodland and related areas (Hiraoka et al., 2007; Shimada et al., 2003).

Ticks are capable of transmitting infectious diseases to cats and humans, therefore, tick infestation is a matter of concern for animal and human health. Various pathogens have been isolated from infested ticks on cats. *Borrelia* spp., a gram-negative anaerobic spirochete bacteria, was detected from *I. granulatus* that was collected from cats in Okinawa, Japan (Hiraoka et al., 2007). In USA, protozoal *Cytauxzoon felils* was found in cats that were infested with *A. americanum* or *Dermacentor variabilis* (MacNeill et al., 2015).

Ticks and other ectoparasites are not only nuisances to both cats and owners, but also significant vectors of many pathogens as previously described. Therefore, safe and convenient tick prevention and control on cats are important to protect cats from infestation by this parasite and reduce the risk of zoonotic transmission. There are various methods and acaricides used for ectoparasite control on cats but spot-on product is one of the most common used by cat owners (Baker et al., 2014; Dryden et al., 2007[a]; Dryden et al., 2007b; Dryden et al., 2013; Kuzner et al., 2013; Matos et al., 2015; Ross et al., 2012). This study was conducted to investigate the possibility of *R. sanguineus* to infest on cats and the efficacy of fipronil spot-on for treatment and control of tick infestation on cats.

Materials and Methods

Experimental animals: Twelve mixed-breed and short-hair cats of both sex (8 females and 4 males), various weights, and more than one year old were used in this study. They were randomly allocated into two groups which were the treatment and control groups. This study was approved by the Chulalongkorn University Animal Care and Use Committee (Animal Use Protocol and Approval No. 1431113).

Ticks: A Thai strain of laboratory-reared brown dog ticks (*Rhipicephalus sanguineus*) was used in this study. They were reared and maintained at the parasitology laboratory, Parasitology Unit, Department of Veterinary Pathology, Faculty of Veterinary Science, Chulalongkorn University. Two- to three-week-old adult ticks were used in this study.

Tested substance: Ten percent w/v fipronil spot-on (Fiproline Spot On Cat, Thainaoka Pharmaceutical, Thailand, Lot No. R&D 03/02/15 Mfg. Date 26/02/2015) was used in this study. A dose of 6.7 mg fipronil per kg body weight was applied on the skin of the cats at the base of the neck between the shoulder blades on day 0 in the treatment group.

Experimental design and data analysis: The 12 cats in this study were randomly allocated into the two groups, six cats per group. All cats were free from any acaricide for at least three months. The control group did not receive any fipronil during the study while the treatment group received fipronil spot-on (Fiproline Spot On Cat) on day 0. The cats were sedated with xylazine HCl (2 mg/kg body weight) and a group of 30 male and 30 female *Rhipicephalus sanguineus* was allowed to feed on each sedated cat on days -7, -2, 3, 7, 14, 21, and 28. The ticks were counted and removed on days -4, 3, 6, 10, 17, 24, and 31. The infested ticks on the cats were also counted but not removed on day 0.

Geometric mean number of attached ticks between the control and treatment groups was compared by using t-test. Fipronil efficacy was calculated using the following formula:

$$\text{Fipronil efficacy (\%)} = \frac{\text{(Geometric mean control – Geometric mean treatment)}}{\text{Geometric mean control}} \times 100$$

Geometric mean control = geometric mean number of infested ticks on untreated control cats at each individual assessment day

Geometric mean treatment = geometric mean number of infested ticks on fipronil-treated cats at each individual assessment day

Blood was collected from each cat before (day 0) and after (day 31) the study. It was tested for complete blood count, creatinine, BUN, SGPT, and alkaline phosphatase to indicate kidney and liver functions. Skin rash on the treatment group was also investigated. Tick infestation was considered successful when attachment rates were equal or more than 25%. For all analyses, a *p*-value threshold was set to 0.05.

Results and Discussion

The 12 domestic short-hair cats in this study were randomly allocated into two groups, the control group and treatment group, which consisted of 6 cats each. The control group did not received any fipronil during the study, whereas the treatment group received fipronil spot-on. Body weight of the control group ranged from 2.8 to 4.9 kg while that of the treatment group ranged from 2.4 to 4.6 kg. A group of 30 male and 30 female *Rhipicephalus sanguineus* was released on each cat on days -7, -2, 3, 7, 14, 21, and 28. The infested ticks were counted and removed on days -4, 3, 6, 10, 17, 24, and 31. The infested ticks on the cats were also counted but not removed on day 0.

The geometric mean number of tick infestation in the control group ranged from 20.83 to 26.17 ticks per cat, or the attachment rate of 34.72 to 43.62% and the mean attachment rate of 39.41%. The geometric mean number of tick infestation in the treatment group on the days before fipronil was applied on the cats ranged from 24.50 to 25.83 ticks per cat, or the attachment rate of 40.83 to 43.06% and the mean attachment rate of 41.95%. The geometric mean numbers of ticks between the control and treatment groups were compared on day -4 and day 0 to indicate that there was no difference between tick feeding and attachment between the groups of cats. In this study, there was no statistically significant difference in the geometric mean numbers of ticks between the control and treatment groups on day -4 ($p = 1.0000$) and day 0 ($p = 0.8576$).

Percentages of the efficacy of fipronil used in this study were 99.24, 100, 100, 100, 99.18, and 99.24% on days 3, 6, 10, 17, 24, and 31, respectively. There were statistically significant differences between the geometric mean numbers of tick between the control and treatment groups on days 3, 6, 10, 17, 24, and 31 ($p < 0.0001$) (Table 1). There was no significant difference in the complete blood count and kidney and liver functions before and after the study. No skin reaction was shown in the treatment group after fipronil was applied on the cats. There are different combinations and formulations of spot-on products used on cats. The different formulations also have different levels of efficacy and duration for ectoparasite prevention and control (Dryden et al., 2007[a]; Dryden et al., 2013; Iannino et al., 2013; Kuzner et al., 2013). The efficacy of each formulation is based on chemistry and quality of active ingredients. The active ingredient of the spot-on used in this study is the same as other fipronil spot-on products in the market, but the other ingredients differ, depending on the manufacturers. Therefore, the immediate and persistent efficacy of each fipronil spot-on product may vary and need to be evaluated before the product can be used on cats. Only few studies were conducted to test the efficacy of fipronil against tick infestation on cats. This study was performed to examine the efficacy of fipronil spot-on to prevent and control brown dog tick infestation on cats.

Table 1 Percentages of efficacy of 10% w/v fipronil spot-on (Fiproline Spot On Cat) against *Rhipicephalus sanguineus* on cats on days 3, 6, 10, 17, 24, and 31 which received fipronil at dose of 0.067 ml/kg body weight (equivalent to fipronil 6.7 mg/kg) on day 0

Tick released day	Tick counted day	Geometric mean number of attached ticks		Tick attachment rate		*p*-value*	Percent Efficacy
		Control group	Treatment group	Control group	Treatment group		
Day-7	Day-4	24.50	24.50	40.83	40.83	1.0000	-
Day-2	Day 0	25.50	25.83	42.50	43.06	0.8576	-
	Day 3	22.33	0.17	37.22	0.28	<0.0001	99.24
Day 3	Day 6	26.17	0	43.62	0	<0.0001	100
Day 7	Day 10	24.33	0	40.55	0	<0.0001	100
Day 14	Day 17	23.00	0	38.33	0	<0.0001	100
Day 21	Day 24	20.83	0.17	34.72	0.28	<0.0001	99.18
Day 28	Day 31	22.50	0.17	37.50	0.28	<0.0001	99.24

*Comparison of mean numbers of ticks between the control and treatment groups

Cats infested with *Rhipicephalus sanguineus* and kept indoors in a laboratory condition were used for testing the efficacy of fipronil spot-on. A group of 30 male and 30 female ticks was directly released on the sedative cats. In this study, not all released ticks attached to and fed on the cats. The geometric mean number of tick infestation in the control group ranged from 20.83 to 26.17 ticks per cat with the attachment rate of 34.72 to 43.62%. The cats infested with ticks also showed the sign of skin reaction at the tick biting sites particularly at the end of the study. The study by Kuzner et al. (2013) indicated that castor bean tick (*Ixodes ricinus*) attachment rate on cats ranged from 29% to 62%.

This study was performed to examine the immediate and persistent effectiveness of fipronil spot-on product against *R. sanguineus*. The efficacy of fipronil (Fiproline Spot On Cat) on days 3, 6, 10, 17, 24, and 31 post fipronil application was higher than 99% with the range between 99.18 and 100%. This study indicates that fipronil has immediate and persistent efficacy against *R. sanguineus* infestation on cats for at least 4 weeks.

A study conducted at the same laboratory and with the same condition found that geometric mean number of tick infestation in the control group ranged from 16.67 to 24.50 ticks per dog and the attachment rate ranged from 27.78 to 40.83%. Percentages of the efficacy of fipronil against *R. sanguineus* infestation on dogs were 71.77, 96.03, 100, 91.84, and 90.21% on days 3, 10, 17, 24, and 31 post fipronil application, respectively (Tiawsirisup et al., 2013).

The findings from this current study are similar to those of Kuzner et al. (2013). They

demonstrated that the efficacy of 50 mg fipronil per cat (10.6-23.8 mg/kg) against cat fleas (*Ctenocephalides felis*) and *I. ricinus* on day 2 post fipronil application was 100 and 94%, respectively. The efficacy of this fipronil formulation lasted for up to 5 weeks against fleas and up to 4 weeks against ticks, and was equal or higher than 96% and equal or higher than 94%, respectively.

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References

Baker C, Tielemans E, Prullage JB, Chester ST, Knaus M, Rehbein S, Fourie JJ, Young DR, Everett WR and Rosentel JK 2014. Efficacy of a novel topical combination of fipronil, (S)-methoprene, eprinomectin and praziquantel against adult and immature stages of the cat flea (*Ctenocephalides felis*) on cats. Vet Parasitol. 202(1-2): 64-68.

Changbunjong T, Sangkachai N and Tangsudjai S 2011. First report of *Ctenocephalides felis* felis on the Asiatic Golden Cat, *Catopuma temminckii* in Thailand. Southeast Asian J Trop Med Public Health. 42(3): 539-541.

Chomel BB, Kasten RW, Floyd-Hawkins K, Chi B, Yamamoto K, Roberts-Wilson J, Gurfield AN, Abbott RC, Pedersen NC and Koehler JE 1996. Experimental transmission of *Bartonella henselae* by the cat flea. J Clin Microbiol. 34(8): 1952-1956.

Claerebout E, Losson B, Cochez C, Casaert S, Dalemans AC, De Cat A, Madder M, Saegerman C, Heyman P and Lempereur L 2013. Ticks and associated pathogens collected from dogs and cats in Belgium. Parasit Vectors. 6: 183. doi:10.1186/1756-3305-6-183.

Dryden M, Payne P, Lowe A, Mailen S, Smith V and Rugg D 2007[a]. Efficacy of a topically applied formulation of metaflumizone on cats against the adult cat flea, flea egg production and hatch, and adult flea emergence. Vet Parasitol. 150(3): 263-267.

Dryden M, Payne P and Smith V 2007[b]. Efficacy of selamectin and fipronil-(S)-methoprene spot-on formulations applied to cats against adult cat fleas (*Ctenocephalides felis*), flea eggs, and adult flea emergence. Vet Ther. 8(4): 255-262.

Dryden MW, Payne PA, Smith V, Heaney K and Sun F 2013. Efficacy of indoxacarb applied to cats against the adult cat flea, *Ctenocephalides felis*, flea eggs and adult flea emergence. Parasit Vectors. 6: 126. doi:10.1186/1756-3305-6-126.

Hiraoka H, Shimada Y, Sakata Y, Watanabe M, Itamoto K, Okuda M, Masuzawa T and Inokuma H 2007. Detection of *Borrelia garinii*, *Borrelia tanukii* and *Borrelia* sp. closely related to *Borrelia valaisiana* in Ixodes ticks removed from dogs and cats in Japan. Vet Parasitol. 144(1-2): 188-192.

Iannino F, Iannetti L, Paganico D and Podaliri Vulpiani M 2013. Evaluation of the efficacy of selamectin spot-on in cats infested with *Aelurostrongylus abstrusus* (Strongylida, Filariodidae) in a Central Italy cat shelter. Vet Parasitol. 197(1-2): 258-262.

Jeffery J, Norhidayu S, Mohd Zain SN, Noor Hayati MI and Nurazila B 2012. The cat fur mite, *Lynxacarus radovskyi* Tenorio, 1974 (Acarina: Astigmata: Listrophoridae) from cat, *Felis catus* in peninsular Malaysia. Trop Biomed. 29(2): 308-310.

Kuzner J, Turk S, Fourie JJ, Grace S, Marchiondo AA and Rugg D 2013. Efficacy of a novel fipronil spot-on for the treatment and control of induced infestations of adult cat fleas (*Ctenocephalides felis*) and castor bean ticks (*Ixodes ricinus*) on cats. Parasitol Res. 112(1): 365-372.

MacNeill AL, Barger AM, Skowronski MC, Lanka S and Maddox CW 2015. Identification of *Cytauxzoon felis* infection in domestic cats from southern Illinois. J Feline Med Surg. doi:10.1177/1098612X14567158.

Matos M, Alho AM, Owen SP, Nunes T and Madeira de Carvalho L 2015. Parasite control practices and public perception of parasitic diseases: A survey of dog and cat owners. Prev Vet Med. doi:10.1016/j.prevetmed.2015.09.006.

Mendes-de-Almeida F, Crissiuma AL, Gershony LC, Willi LM, Paiva JP, Guerrero J and Labarthe N 2011. Characterization of ectoparasites in an urban cat (*Felis catus* Linnaeus, 1758) population of Rio de Janeiro, Brazil. Parasitol Res. 108(6): 1431-1435.

Ogden NH, Cripps P, Davison CC, Owen G, Parry JM, Timms BJ and Forbes AB 2000. The ixodid tick species attaching to domestic dogs and cats in Great Britain and Ireland. Med Vet Entomol. 14(3): 332-338.

Ross DH, Arther RG, von Simson C, Doyle V and Dryden MW 2012. Evaluation of the efficacy of topically administered imidacloprid + pyriproxyfen and orally administered spinosad against cat fleas (*Ctenocephalides felis*): Impact of treated dogs on flea life stages in a simulated home environment. Parasit Vectors. 5: 192. doi:10.1186/1756-3305-5-192.

Shaw SE, Kenny MJ, Tasker S and Birtles RJ 2004. Pathogen carriage by the cat flea *Ctenocephalides felis* (Bouche) in the United Kingdom. Vet Microbiol. 102(3-4): 183-188.

Shimada Y, Inokuma H, Beppu T, Okuda M and Onishi T 2003. Survey of ixodid tick species on domestic cats in Japan. Vet Parasitol. 111(2-3): 231-239.

Slapeta J, King J, McDonell D, Malik R, Homer D, Hannan P and Emery D 2011. The cat flea (*Ctenocephalides f. felis*) is the dominant flea on domestic dogs and cats in Australian veterinary practices. Vet Parasitol. 180(3-4): 383-388.

Tiawsirisup S, Thiansirikhun K, Thanadumkerng K, Pastarapatee N, Trirattananuwong N and Rattanatayarom W 2013. Antiparasitic efficacy of Fiproline Spot On (10% w/v fipronil spot on) against experimental tick (*Rhipicephalus sanguineus*) infestations on dogs. Thai Journal Vet Med. 43(2): 279-284.

Wedincamp J Jr and Foil LD 2002. Vertical transmission of *Rickettsia felis* in the cat flea (*Ctenocephalides felis* Bouche). J Vector Ecol. 27(1): 96-101.

Youssefi MR, Ebrahimpour S, Rezaei M, Ahmadpour E, Rakhshanpour A and Rahimi MT 2014. Dermatitis caused by *Ctenocephalides felis* (cat flea) in human. Caspian J Intern Med. 5(4): 248-250.

Youssefi MR and Rahimi MT 2014. Extreme human annoyance caused by *Ctenocephalides felis felis* (cat flea). Asian Pac J Trop Biomed. 4(4): 334-336.

บทคัดย่อ

ประสิทธิภาพของฟิโปรนิล สปอต ออน 10% ในการกำจัดและป้องกันเห็บ *Rhipicephalus sanguineus* บนแมว

สนธยา เตียวศิริทรัพย์[1*] วิไล รัตนตยารมณ์[2*]

ศึกษาประสิทธิภาพของฟิโปรนิล 10% รูปแบบหยดหลังในการกำจัดและป้องกันเห็บ *Rhipicephalus sanguineus* บนแมว การศึกษานี้ประกอบไปด้วยแมวจำนวน 12 ตัว โดยแบ่งแมวออกเป็น 2 กลุ่ม คือ กลุ่มทดลองและกลุ่มควบคุม ในวันที่ 0 กลุ่มทดลองได้รับฟิโปรนิล 10% ในขนาด 6.7 มิลลิกรัมต่อกิโลกรัม ทำการปล่อยเห็บลงบนตัวแมวในวันที่ -7, -2, 3, 7, 14, 21 และ 28 และทำการนับเห็บบนตัวแมวและเก็บเห็บออกจากแมวในวันที่ -4, 3, 6, 10, 17, 24 และ 31 รวมทั้งทำการนับเห็บบนตัวแมวแต่ไม่เก็บเห็บออกจากแมวในวันที่ 0 การศึกษาพบว่าค่าเฉลี่ยของจำนวนเห็บบนแมวในกลุ่มควบคุมอยู่ระหว่าง 20.83-26.17 ตัว หรือคิดเป็นร้อยละ 34.72-43.62 หรือมีค่าเฉลี่ยอยู่ที่ร้อยละ 39.41 สำหรับกลุ่มทดลอง ค่าเฉลี่ยของจำนวนเห็บบนตัวแมวก่อนการหยดยาอยู่ระหว่าง 24.50-25.83 ตัว หรือคิดเป็นร้อยละ 40.83-43.06 หรือมีค่าเฉลี่ยอยู่ที่ร้อยละ 41.95 ประสิทธิภาพของฟิโปรนิลในการกำจัดและป้องกันเห็บบนแมวนั้นมีค่าร้อยละ 99.24, 100, 100, 100, 99.18 และ 99.24 ในวันที่ 3, 6, 10, 17, 24 และ 31 ตามลำดับ ค่าเฉลี่ยของเห็บในกลุ่มทดลองและกลุ่มควบคุมในวันที่ 3, 6, 10, 17, 24 และ 31 มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ

คำสำคัญ: ประสิทธิภาพ ฟิโปรนิลรูปแบบหยดหลัง เห็บ แมว

[1]กลุ่มการวิจัยโรคติดเชื้อในสัตว์ที่มีพาหะนำโรค หน่วยปรสิตวิทยา ภาควิชาพยาธิวิทยา คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
[2]ภาควิชาเภสัชวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ
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