

# Categorization of antimicrobial agents prescribed in the Veterinary Teaching Hospital in Thailand

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## Abstract

Antimicrobial resistance (AMR) is critical situation for human and animal health worldwide. The inappropriate antimicrobial use is one of the risk factors of AMR. Intriguingly, an increase of antimicrobial resistance bacteria was recently evident in companion animals. Since such circumstance strongly implied the contribution of inappropriate antimicrobial use in veterinary clinics and hospitals to the problems, this study aimed to categorize and evaluate antimicrobials prescribed in the Veterinary Teaching Hospital in Thailand. From 6,200 animal patients, there were total 8,093 antimicrobial prescriptions for animal treatments. The antimicrobials were prescribed for parenteral administrations 3,346 prescriptions (41.3%) and oral administrations 4,747 prescriptions (58.7%), respectively. During 2012-2015, the most antimicrobial prescriptions were enrofloxacin (33.9%,  $P<0.001$ ) with significantly difference from amoxicillin/clavulanate (24.1%) and doxycycline (15.2%). Enrofloxacin was highest prescribed in both parenteral and oral administrations (41.2% and 28.8%, respectively). Surgical procedure was topmost of parenteral antimicrobial prescriptions (16.5%,  $P<0.05$ ), especially for neutering cases, followed with gastrointestinal system (14.6%) and dermatological system (9.5%). The most oral antimicrobial prescriptions were used for treatments of dermatological system (16.3%,  $P<0.05$ ), gastro-intestinal system (11.1%) and surgical procedures (8.9%). These study revealed the pattern of antimicrobial use in companion animals to fulfill the associated picture with AMR problem in Thailand, and underline requirement of better solving plan based on one health approach with more concern of antimicrobial use in veterinary fields.

**Keywords:** antimicrobial prescriptions, antimicrobial resistance, companion animals, Thailand

# การจำแนกการส่งจ่ายยาต้านจุลชีพเพื่อใช้ในโรงพยาบาลสัตว์ เพื่อการเรียนการสอนในประเทศไทย

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## บทคัดย่อ

การดื้อยาต้านจุลชีพเป็นสถานการณ์วิกฤตที่ส่งผลกระทบต่อสุขภาพของมนุษย์และสัตว์ทั่วโลก การใช้ยาต้านจุลชีพที่ไม่เหมาะสมเป็นปัจจัยสำคัญที่ทำให้เกิดปัญหาการดื้อยาต้านจุลชีพ ปัจจุบันนี้มีการพบแบคทีเรียที่ดื้อยาต้านจุลชีพในสัตว์เลี้ยงเพิ่มขึ้น ซึ่งการใช้ยาต้านจุลชีพอย่างไม่เหมาะสมในโรงพยาบาลและคลินิกรักษาสัตว์ มีส่วนเกี่ยวข้องกับปัญหาดังกล่าว การศึกษาครั้งนี้ จึงมีจุดประสงค์ในการเก็บรวบรวมข้อมูล และจัดกลุ่มการส่งจ่ายยาต้านจุลชีพในโรงพยาบาลสัตว์เพื่อการเรียนการสอนในประเทศไทย ระหว่างปี พ.ศ. 2555-2558 จากข้อมูลสัตว์ป่วยจำนวน 6,200 ตัว พบว่า มีการส่งจ่ายยาต้านจุลชีพ 8,093 ครั้ง เป็นการส่งจ่ายฉีดในสัตว์ป่วย 3,346 ครั้ง (ร้อยละ 41.3) และยากิน 4,747 ครั้ง (ร้อยละ 58.7) ยาต้านจุลชีพที่มีการสั่งใช้สูงสุดอย่างมีนัยสำคัญทางสถิติ คือ enrofloxacin (ร้อยละ 33.9 ค่า  $P < 0.001$ ) ตามด้วย amoxicillin/clavulanate (ร้อยละ 24.1) และ doxycycline (ร้อยละ 15.2) ซึ่ง enrofloxacin นั้น ถูกสั่งใช้มากที่สุด ทั้งรูปแบบยาฉีดและยากิน (ร้อยละ 41.2 และ 28.8 ตามลำดับ) สัตว์ป่วยส่วนใหญ่ได้รับยาต้านจุลชีพรูปแบบการฉีดมากที่สุดในกระบวนการคัดลอกกรรม (ร้อยละ 16.5 ค่า  $P < 0.05$ ) โดยเฉพาะการผ่าตัดทำหมัน รองลงมาคืออาการหรือโรกระบบทางเดินอาหาร (ร้อยละ 14.6) และความผิดปกติที่ผิวหนัง (ร้อยละ 9.5) ยาต้านจุลชีพแบบกินถูกสั่งใช้มากที่สุดเพื่อรักษาความผิดปกติที่ผิวหนัง (ร้อยละ 16.3 ค่า  $P < 0.05$ ) ระบบทางเดินอาหาร (ร้อยละ 11.1) และการทำคัดลอกกรรม (ร้อยละ 8.9) ผลการศึกษาแสดงให้เห็นถึงรูปแบบการสั่งจ่ายยาต้านจุลชีพในสัตว์เลี้ยง ซึ่งข้อมูลดังกล่าวจะช่วยให้เห็นภาพรวมของปัญหาการดื้อยาต้านจุลชีพในประเทศไทยได้ชัดเจนยิ่งขึ้น สัตวแพทย์ที่มีความรู้และความตระหนักถึงปัญหาดังกล่าว มีส่วนสำคัญในการช่วยแก้ไขและลดความรุนแรงของปัญหาตามพื้นฐานของสุขภาพแบบองค์รวมได้

คำสำคัญ: การสั่งจ่ายยาต้านจุลชีพ การดื้อยาต้านจุลชีพ สัตว์เลี้ยง ประเทศไทย

## INTRODUCTION

The antimicrobials have been highly used in both human and animals. The previous data showed the increasing of antimicrobial consumption by 36% between 2000 and 2010 (Van Boeckel et al., 2014). For decades, the incidences of AMR have become critical problem in food-producing animals (Gould, 2009; Wilcox, 2009). Pathogenic bacteria can develop the antimicrobial resistance through several biological mechanisms such as gene mutations, over-expression of efflux pumps, and protection of the drug target sites by protein modification (Munita and Arias, 2016). The antimicrobial resistance gene carried bacteria have been recently isolated from companion animals (Guardabassi et al., 2004). In 2009, isolations of extended  $\beta$ -lactamase producing (ESBL) *Escherichia coli*, methicillin-resistant *Staphylococcus aureus* (MRSA), and methicillin-resistant *S. pseudintermedius* (MRSP) were surprisingly archived among healthy dogs and cats (Murphy et al., 2009). In Thailand, ESBL-producing *Enterobacteriaceae* in fecal carriage from healthy stray dog, household dog and shelter dog samples were reported (62%, 8% and 70.1%, respectively). Furthermore, the MRSA and some antimicrobial resistance *E. coli* were also presented. (Boonmasawai et al., 2017, Boonmasawai et al., 2018). Since inappropriate antimicrobial prescriptions in human are well regarded as a major contributor to antimicrobial resistance development, (Castro-Sánchez et al., 2016; Granov et al., 2016), inappropriate antimicrobial prescriptions should contribute to the antimicrobial resistance in companion animals, as well. The veterinarians, one of the key prescriber also have much effects on AMR problem (Zhuo et al., 2018). By means of this, this study aimed to address the antimicrobial prescriptions in companion animals from

the Veterinary Teaching Hospital in Thailand during 2012-2015. The expected data will show the pattern of antimicrobial prescription in each year and the antimicrobial use in each group of clinical problems. These gathering data of antimicrobial use have been required for weaving the overall picture of AMR problem and leading to rational antimicrobial guidelines in veterinary fields.

## METHODOLOGY

This study was a retrospective cohort study that randomly collected the data of antimicrobial prescription by veterinarians for companion animals from outpatient department (OPD) cards. These animal patients obtained medications between January 1<sup>st</sup>, 2012 to December 31<sup>st</sup>, 2015 at Prasu-Arthorn Veterinary Teaching Hospital, Faculty of Veterinary Science, Mahidol University, Thailand. The general information of the patients; sex, breed, age, weight and living places was recorded. The medical history of patient was summarized and then categorized into 13 groups according to major clinical problem as following gastrointestinal system (G), respiratory system (R), dermatological system (D), urinary system (U), cardiovascular system (CV), reproductive system (RP), neurological system (NU), sensory organs (SO), musculoskeletal system (MU), neoplasm (Neo), surgical procedure (S), blood parasite infection (BP) and other cases (O), accordingly (Nelson and Couto, 2014). All the antimicrobial prescription data by veterinarians were descriptive analyzed by IBM SPSS Statistics 23.0. The significance of differences between groups was evaluated using the *Chi-square* test (significance level set at  $P < 0.05$ )

## RESULTS

The number of records in each year was 2,400, 1,400, 1,200 and 1,200 cases, respectively (2012 -2015). The animal patients were living in Bangkok (52.4%, 3,247 cases), Nakhon Pathom (19.5%, 1,211 cases), Nonthaburi (15.1%, 939 cases) and other provinces (13%, 803 cases). The species of animals were dogs (77%, 4,776 cases), cats (18.3%, 1,135 cases), and other species such as rabbit, ferret, bird, chicken, hamster, guinea pig, turtle, snake, etc. (4.7%, 289 cases). From 6,200 animal patients, there were 2,930 females (47.3%) and 3,193 males (51.5%). Some bird, turtle and snake were not identified the sexual status (77 animals, 1.2%). The age 57.8 month (range: 1-264 months) and weight 10.3 kg (range: 0.02-62 kg) were averages of all.

There were total 8,093 antimicrobial prescriptions by veterinarians for animal treatments. The antimicrobials were prescribed for parenteral administrations 3,346 prescriptions (41.3%) and oral administrations 4,747 prescriptions (58.7%), respectively. Some patients received one or more parenteral prescriptions and oral prescriptions at the same time (Table 1). The three order prescribed antimicrobials every year during 2012-2015 were enrofloxacin, amoxicillin/clavulanate and doxycycline (Figure 1). From total prescribed antimicrobials, the first order prescribed antimicrobial was also enrofloxacin (33.9%,  $P<0.001$ ) with significantly difference from the second and third order prescribed antimicrobials. By classification according to molecular structure and antimicrobial mechanisms, the fluoro-quinolone (40.2%): enrofloxacin, marbofloxacin norfloxacin and ciprofloxacin was frequency prescribed when compared with others ( $P<0.05$ ) (Figure 2).

The parenteral prescriptions of antimicrobials were shown in figure 3. Enrofloxacin (41.2%,  $P<0.001$ )

was mostly chosen by veterinarians with significantly difference from amoxicillin/clavulanate (28%) and marbofloxacin (8.7%). By oral administration, the enrofloxacin was the chosen one for animal treatments (28.8%,  $P<0.05$ ) more than doxycycline (25.9%) and the combination of amoxicillin and clavulanate (21.4%) (Figure 4).

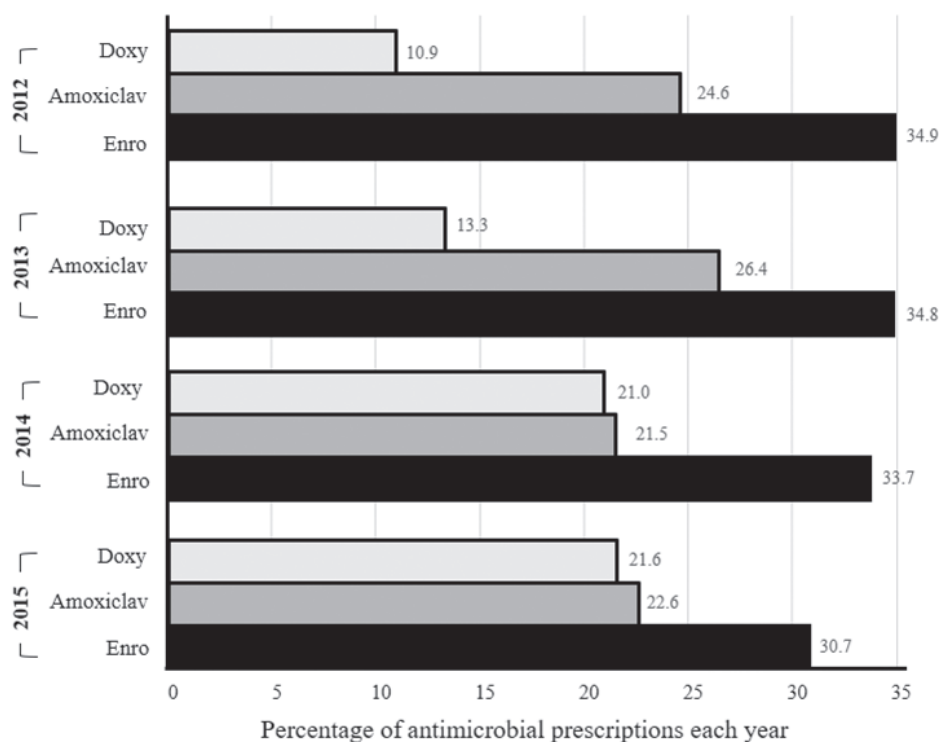
The topmost clinical problems of animal patients receiving antimicrobial injections were during surgical procedure (16.5%,  $n=552$ ) (Table 2). The parenteral antimicrobial using for pre-operative antimicrobial prophylaxis in neutering cases had the highest rate (47.1%,  $n=260$ ). The percentage of antimicrobial uses for treatment of orthopedic and reproductive cases before and after surgery were comparable (13.2%,  $n=73$ ), the remaining cases were eye surgical procedure, gastrotomy, perineal hernia. etc. Within surgical group, the most injected antimicrobials were enrofloxacin ( $P<0.05$ ), amoxicillin/clavulanate and cefazolin (29%, 26.3% and 25.7%, respectively). In gastrointestinal system (14.6%,  $n=488$ ), by 83.9% of animals had diarrhea symptoms. The data revealed that parenteral enrofloxacin was mostly used to cure animals in this group ( $P<0.001$ ), followed with amoxicillin/clavulanate and trimethoprim/sulfamethoxazole (63.4%, 13.3% and 12.6%, respectively). In dermatological system, bacterial infection was the major causes of veterinarian treatment decisions (55.7%,  $n=177$ ). The bite-open wound also highly found (28.3%,  $n=90$ ). Other causes of dermatological symptom were allergy and skin mass, etc. The parenteral amoxicillin/clavulanate was highly chosen to treat bacterial dermatological infection (52.3%) ( $P<0.05$ ), followed with enrofloxacin and marbofloxacin (27.6% and 7.2%, respectively).

According to the clinical signs, the most oral antimicrobial prescriptions were used for treatments of dermatological system (16.3%, n=774,  $P<0.001$ ), gastrointestinal system (11.1%, n=527) and surgical procedure (8.9%, n=422) (Table 3). The veterinarians determined to use oral antimicrobials for animals with bacterial infection on skin (34%, n= 263) such as skin abscess, pyoderma, etc. The oral antimicrobials for bite-open wound treatments often prescribed to animals (16.7%, n=129). The most oral prescribed antimicrobials of which were cephalixin (38.4%,  $P<0.05$ ), amoxicillin/clavulanate acid (22.3 %), and enrofloxacin (12.7 %).

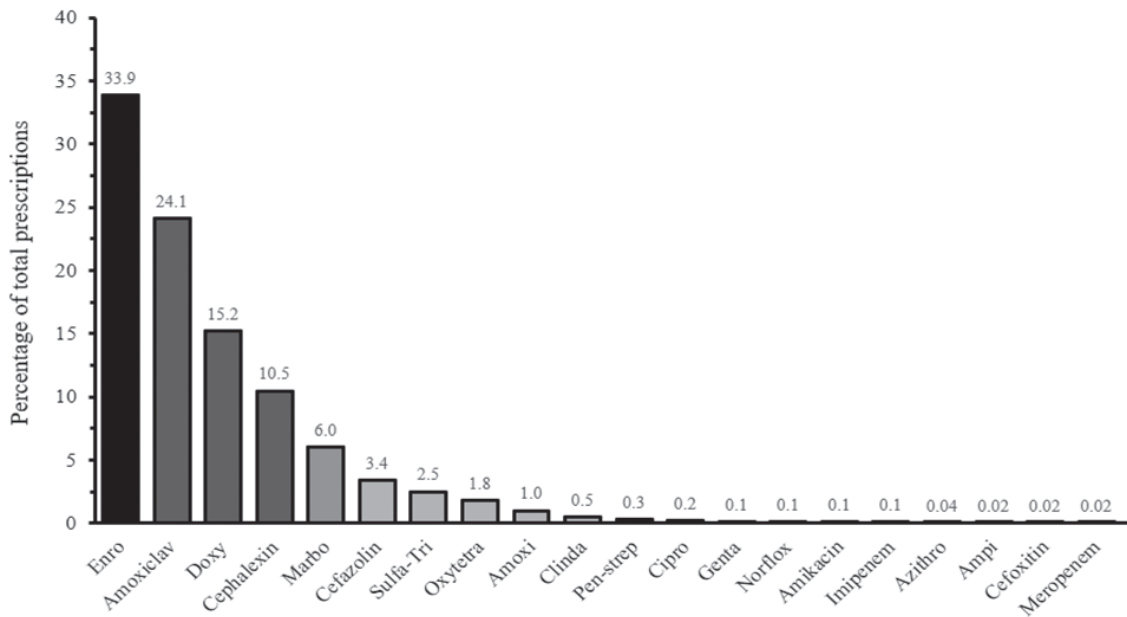
The symptom of patients in gastrointestinal system located in stomach and small intestine (81.6%, n=430), dental and buccal cavity (13.8%, n=73) and large

intestine and anus (4.6%, n=24). The most oral prescribed antimicrobials of which were enrofloxacin (27.6%,  $P<0.05$ ), trimethoprim/ sulfamethoxazole (27.3 %) and amoxicillin/clavulanate (11.8 %).

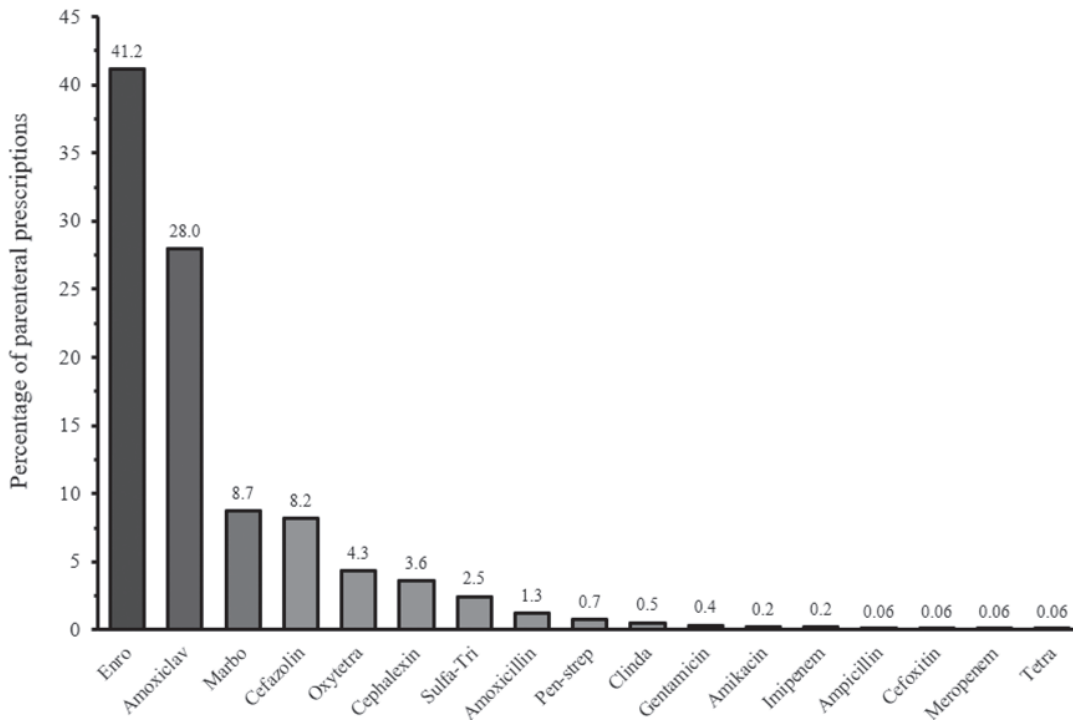
Like the parenteral prescriptions, oral prescriptions for preoperative antimicrobial prophylaxis for neutering cases had the highest rate in surgical procedure (15.2%, n=64). The oral antimicrobials were also highly given after surgical procedure of infectious reproductive system such as canine and feline pyometra (13.3%, n=56) and tumor (11.8%, n=50). The most oral prescribed antimicrobials of which were cephalixin (29.7%), enrofloxacin (26.2%) and amoxicillin/clavulanate (21.5 %).



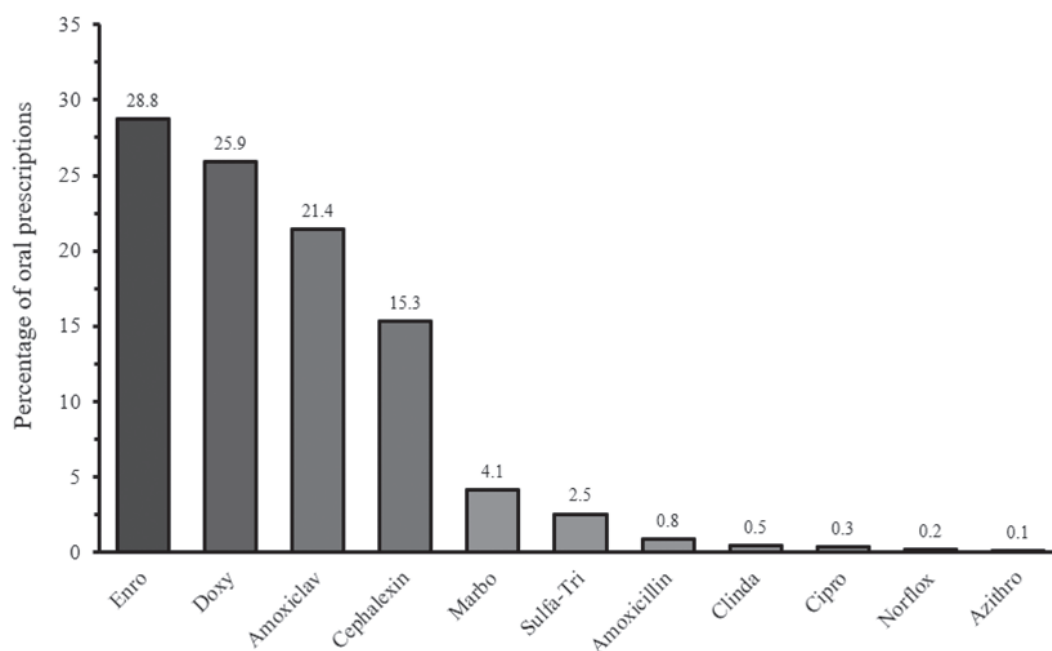
**Figure 1** The third most antimicrobial prescriptions from the Veterinary Teaching Hospital OPD records in 2012 (n=3,278), 2013 (n=1,910), 2014 (n=1,422) and 2015 (n=1,483), Percentage of antimicrobial prescriptions calculated from total prescriptions each year.



**Figure 2** The antimicrobial prescriptions for animal treatments in the Veterinary Teaching Hospital during 2012 - 2015, Percentage of antimicrobial prescriptions calculated from total 8,093 prescriptions.



**Figure 3** The percentage of parenteral antimicrobial prescriptions for animal treatments in the Veterinary Teaching Hospital during 2012 - 2015 (Total prescriptions =3,346).



**Figure 4** The percentage of oral antimicrobial prescriptions for animal treatments in the Veterinary Teaching Hospital during 2012 - 2015 (Total prescriptions =4,747).

**Table 1** The number of animals and antimicrobial prescriptions for oral and parenteral administration in the Veterinary Teaching Hospital during 2012 - 2015, n=number of antimicrobial prescriptions.

Antimicrobial prescriptions			Year							
			2012		2013		2014		2015	
1'	2'	Oral	animals	n	animals	n	animals	n	animals	n
parenteral	parenteral	-	522	522	241	241	210	210	173	173
✓	-	-	73	146	61	122	14	28	5	10
✓	✓	✓	33	99	49	147	7	21	3	9
✓	-	✓	739	1478	351	702	194	388	272	544
-	-	✓	1033	1033	698	698	775	775	747	747
<b>Sum</b>			2400	3278	1400	1910	1200	1422	1200	1483

**Table 2** The third most parenteral antimicrobial prescriptions according to the clinical sign categorization (Total prescriptions =3,346).

Categorized clinical signs	Prescriptions		The most prescribed antimicrobials					
	n	(%)	1'	(%)	2'	(%)	3'	(%)
S	552	(16.5)	Enro	(29.0)	Amoxiclav	(26.3)	Cefazolin	(25.7)
G	488	(14.6)	Enro	(63.4)	Amoxiclav	(13.3)	Sulfa-Tri	(12.6)
D	318	(9.5)	Amoxiclav	(52.3)	Enro	(27.6)	Marbo	(7.2)
U	311	(9.3)	Enro	(58.8)	Amoxiclav	(28.1)	Marbo	(7.7)
O	281	(8.4)	Enro	(50.8)	Amoxiclav	(20.7)	Marbo	(11.0)
MU	264	(7.9)	Amoxiclav	(44.0)	Enro	(27.6)	Cefazolin	(12.5)
R	248	(7.4)	Enro	(41.1)	Amoxiclav	(38.4)	Marbo	(9.1)
RP	221	(6.6)	Enro	(60.4)	Marbo	(18.3)	Amoxiclav	(16.2)
SO	218	(6.5)	Enro	(47.2)	Cefazolin	(16.6)	Amoxiclav	(15.0)
CV	144	(4.3)	Enro	(47.6)	Marbo	(19.8)	Amoxiclav	(19.0)
BP	117	(3.5)	Oxytetra	(56.2)	Enro	(34.3)	Marbo	(5.7)
NEO	104	(3.1)	Enro	(43.3)	Amoxiclav	(35.6)	Marbo	(76.7)
NU	80	(2.4)	Enro	(51.4)	Amoxiclav	(21.4)	Marbo	(10.0)

**Table 3** The third most oral antimicrobial prescriptions according to the clinical sign categorization (Total prescriptions =4,747).

Categorized clinical signs	Prescriptions		The most prescribed antimicrobials					
	n	(%)	1'	(%)	2'	(%)	3'	(%)
D	774	(16.3)	Cephalexin	(38.4)	Amoxiclav	(22.3)	Enro	(12.7)
G	527	(11.1)	Enro	(27.6)	Sulfa-Tri	(27.3)	Amoxiclav	(11.8)
S	422	(8.9)	Cephalexin	(29.7)	Enro	(26.2)	Amoxiclav	(21.5)
BP	418	(8.8)	Doxy	(88.4)	Enro	(3.3)	Marbo	(0.6)
R	413	(8.7)	Amoxiclav	(35.5)	Enro	(21.6)	Doxy	(15.2)
MU	370	(7.8)	Amoxiclav	(20.4)	Cephalexin	(18.6)	Doxy	(18.1)
O	361	(7.6)	Doxy	(26.1)	Enro	(13.6)	Amoxiclav	(13.6)
U	347	(7.3)	Enro	(33.9)	Amoxiclav	(17.8)	Doxy	(9.7)
SO	328	(6.9)	Enro	(33.6)	Cephalexin	(21.6)	Doxy	(16.2)
NEO	285	(6.0)	Amoxiclav	(32.9)	Enro	(22.1)	Doxy	(21)
RP	209	(4.4)	Enro	(25.9)	Amoxiclav	(8.4)	Doxy	(6.9)
CV	199	(4.2)	Doxy	(32.3)	Enro	(21.7)	Amoxiclav	(11.0)
NU	94	(2.0)	Enro	(25.6)	Doxy	(18.4)	Amoxiclav	(16.0)

List of Abbreviation (Figures 1-4 and Tables 2-3) Ampi, ampicillin; Amoxi, amoxicillin; Amoxiclav, amoxicillin/clavulanate; Azithro, azithromycin; Clinda, clindamycin; Cipro, ciprofloxacin; Doxy, doxycycline; Enro; enrofloxacin; Genta, gentamicin; Marbo, marbofloxacin; Norflox, norfloxacin; Oxytetra, oxytetracycline; Pen-strep, Penicillin Streptomycin mixtures; Sulfa-Tri, Trimethoprim/sulfamethoxazole.

## DISCUSSION

From our study, the antimicrobial prescriptions for companion animals in Thailand were firstly recorded and categorized. The most prescribed antimicrobials by veterinarians were enrofloxacin. After the diagnostic procedure, the influenced factors of antimicrobial prescriptions were the results of antimicrobial susceptibility test, veterinarian experiences and the situation of antimicrobial resistance problems. The availability and convenience of antimicrobials in each country were also significant (De Briyne et al., 2013). Therefore, the reasons of highest uses of enrofloxacin might relate to its excellent broad spectrum antimicrobial activities against Gram-negative and Gram positive microbes, beside it has several approved veterinary formulations by in both oral and parenteral dosage forms (FDA, 2018). In Japan, the legal product of enrofloxacin was mostly prescribed by veterinarians for companion animal treatments (Tanaka et al., 2017). All prescriptions of enrofloxacin preparations in our study were the approved veterinary formulations.

Enrofloxacin is the recommended antimicrobials indicated for urinary tract and respiratory infections in dogs and cats (Weese et al., 2011). The surveillance of pathogenic bacteria in Europe during 2008-2010 showed that *E. coli* (52.5%), *Staphylococcus* spp. (13.6%) and *Enterococcus* spp. (13.3%) commonly isolated from urinary tract of dogs and cats had high susceptibility to enrofloxacin (Wong et al., 2015; Moyaert et al., 2017). The amoxicillin/clavulanate susceptibility in dogs was likewise high (98.0%), but *E. coli* had trend to resistant to amoxicillin/clavulanate in cats (Moyaert et al., 2017). Thus amoxicillin/clavulanate was suggested to use against Gram positive, whereas fluoroquinolones were the recommended option for Gram negative in dogs (Rampacci et al., 2018). The data from our study showed

the lower uses of amoxicillin/clavulanate comparing with other countries. (Fig. 2-3). The most prescribed antimicrobials in England and Wales in 2011 were  $\beta$ -lactam antimicrobials (76%) and combinations of amoxicillin and clavulanate (36%) (Radford et al., 2011), as high as USA (Fowler et al., 2015).

The doxycycline was prescribed as the third most used antimicrobials might because it still had high therapeutic efficacy against coagulase-positive staphylococci in dogs (Bean and Wigmore, 2016) and Gram-negative urinary tract infections (UTIs) in dogs and cats (Rampacci et al., 2018). Doxycycline are also suggested to use as a first-line option for secondary bacterial upper respiratory infections (RTIs) (Lappinet al., 2017). The major pathogen isolated bacteria from canine RTIs was *Staphylococcus intermedius* (Morrissey et al., 2016). But *Staphylococcus* spp. isolated from dogs in South Africa during 2007-2012 showed the increasing trend of enrofloxacin resistance. In contrast, the bacterial resistance to doxycycline and amoxicillin/clavulanate significantly decreased (Qekwana et al., 2017). Moreover, doxycycline is frequently chosen for dog treatments because of its other antimicrobial activity for canine blood parasites such as *Ehrlichia canis* (Fourie et al., 2015; Shropshire et al., 2018) and *Hepatozoon canis* (Roopali et al., 2017).

When considering the reasons of antimicrobial prescriptions, the major clinical problems that were mentioned to prescribe antimicrobials were not much difference. The infectious dermatitis was the major clinical sign of dogs and cats from 25 European countries in 2014 that was mentioned to antimicrobial uses (De Briyne et al., 2014). The isolated feline and canine dermatological pathogens were highly susceptible to penicillin, ampicillin, amoxicillin/clavulanate and

fluoroquinolones (Ludwig et al., 2016). The old antibiotics, penicillin were still prescribed in Europe (33% in dogs and 37% in cats), following by cephalosporins and fluoroquinolones (De Briyne et al., 2014). From our study, the injectable penicillin (as penicillin/streptomycin preparation) was less given (0.7%), while the uses of oral penicillin were not found any record in OPD cards. Because of penicillin narrow spectrum, commonly reported drug hypersensitivity and the highly development of  $\beta$ -lactamases-producing bacteria (Wright, 1999), the more efficacy and higher pharmacokinetic property  $\beta$ -lactam antimicrobials were chosen by veterinarian such as ampicillin and cephalosporin in consequence. The isolated bacteria from dog RTIs in Europe still showed Therefore the high ampicillin-susceptibility (Morrissey et al., 2016). In contrast, the previous reports in Thailand showed that the isolated Gram positive and negative bacteria from dog RTIs revealed the resistance to ampicillin (Boonmasawai et al., 2017, Boonmasawai et al., 2018).

The surgical antimicrobial prophylaxis to prevent the infectious complications is usually performed in animal hospitals. (Hardefeldt et al., 2017) There were frequent prescribed antimicrobials for parenteral administration in surgical procedure from our study with enrofloxacin, amoxicillin/clavulanate and cefazolin. Compared with dog patients in UK, the parenteral amoxicillin/clavulanate and second generation cephalosporins such as cefuroxime were high frequency used in preoperative prophylaxis (Gosling and Martinez-Taboada, 2018). The parenteral short half-life cephalosporin such as cefazolin and cefoxitin are generally used as single preoperative dose (Allegranzi et al., 2016). Because all surgical procedures always coincide with high risk of infection as well as the potential risks of antimicrobial resistance (Ierano et al., 2017), the prolongation of antimicrobial uses continuously up to several days

after surgery might leads to serious concerns for the risk of antimicrobial resistance (Cai et al., 2016).

The increasing of ESBL-producing *E. coli* can be found from food-producing animals. The ESBL-producing *E. coli*, MRSA, and MRSP were also found among healthy dogs and cats which close to human (Michael et al., 2017; Boonmasawai et al., 2017; Boonmasawai et al., 2018). While, fluoroquinolone resistance increased in *Enterobacteriaceae* causing community acquired or healthcare associated urinary tract infections and intra-abdominal infections, exceeding 50% in some parts of the world, particularly in Asia (Dalhoff et al., 2019). The strong correlation between the antimicrobial resistant proportion and antimicrobial use was widely observed. The irrational use of antimicrobial agents has an impact on the emergence and dissemination of AMR. The results of highly selective pressure cause further increasing of the last-line antimicrobial consumption. (Wushouer et al., 2015). The antimicrobial prescription surveillance in companion animals in Thailand should be investigated furthermore. Because the rational drug use (RDU) of antimicrobials by responsible veterinarian is critically important for balancing the optimum therapeutic outcome and animal safety. Base on one health concept, the good knowledge, strong attitudes and high-level perceptions of veterinarians as prescriber can drive the improvement of antimicrobial prescribing in practices (Visschers et al., 2016; Asante et al., 2017; Schneider et al., 2018). The essential medicine policies are required to reduce inappropriate antimicrobial use (Holloway et al., 2016). RDU guidelines in companion animals must be equipped for animal treatments. Therefore, the additional data from veterinary fields are urgently required for fulfill the overall pictures to understand and solving AMR problem in Thailand.

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## REFERENCES

- Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis.* 2016; 16(12): e276-87.
- Asante KP, Boamah EA, Abdulai MA, Buabeng KO, Mahama E, Dzabeng F, et al. Knowledge of antibiotic resistance and antibiotic prescription practices among prescribers in the Brong Ahafo Region of Ghana; a cross-sectional study. *BMC Health Serv Res.* 2017; 17(1): 422.
- Bean DC, Wigmore SM. Carriage rate and antibiotic susceptibility of coagulase-positive staphylococci isolated from healthy dogs in Victoria, Australia. *Aust Vet J.* 2016; 94(12): 456-60.
- Boonmasawai S, Bangphoomi N, Sungpradit S, Pati N, Tangkoskul T, Thamlikitkul T. Prevalence of antimicrobial resistant bacteria in dogs resided in central region of Thailand. *Journal of Health Systems Research.* 2017; 11(4): 572-80.
- Boonmasawai S, Bangphoomi N, Sungpradit S, Pati N, Tangkoskul T, Thamthaweechok N, et al. Screening of Antimicrobial Resistant Bacteria in Dog Shelters in Thailand. *J Appli Anim Sci.* 2018; 11(3): 25-36.
- Cai T, Verze P, Brugnolli A, Tiscione D, Luciani LG, Eccher C, et al. Adherence to European association of urology guidelines on prophylactic antibiotics: An important step in antimicrobial stewardship. *Eur Urol.* 2016; 69(2): 276-83.
- Castro-Sánchez E Moore LS, Husson F, Holmes AH. What are the factors driving antimicrobial resistance? Perspectives from a public event in London, England. *BMC Infect Dis.* 2016; 16 (1): 465-70.
- Dalhoff A. Global fluoroquinolone resistance epidemiology and implications for clinical use. *Interdiscip Perspect Infect Dis.* 2012; 2012: 976273-73.
- De Briyne N, Atkinson J, Pokludová L, Borriello SP, Price S. Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe. *Vet Rec.* 2013; 173 (19): 475-82.
- De Briyne N, Atkinson J, Pokludová L, Borriello SP. Antibiotics used most commonly to treat animals in Europe. *Vet Rec.* 2014; 175 (13): 325-33.
- Fourie JJ, Horak I, Crafford D, Erasmus HL, Botha OJ. The efficacy of a generic doxycycline tablet in the treatment of canine monocytic ehrlichiosis. *J S Afr Vet Assoc.* 2015 25; 86(1): 1193.
- Fowler H, Davis MA, Perkins A, Trufan S, Joy C, Buswell M, et al. A survey of veterinary antimicrobial prescribing practices, Washington State 2015. *Vet Rec.* 2015; 179(25): 651-57.
- Gosling MJ and Martinez-Taboada F. Adverse reactions to two intravenous antibiotics (Augmentin and Zinacef) used for surgical prophylaxis in dogs. *Vet Rec.* 2018; 182(3):80-6.

- Gould IM. Antibiotic resistance: the perfect storm. *Int J Antimicrob Agents*. 2009; 34(S3): 2-5.
- Granov D, Ljubovic AD, Zec SL, Granov N, Hukic M. The impact of antibiotic consumption on development of *Acinetobacter Baumannii* resistance. *Mater Sociomed*. 2016; 28(6): 449-53.
- Guardabassi L, Schwarz S, Lloyd DH. Pet animals as reservoirs of antimicrobial resistant bacteria Review. *J Antimicrob Chemother*. 2004; 54(2): 321-32.
- Hardefeldt LY, Browning GF, Thursky K, Gilkerson JR, Billman-Jacobe H, Stevenson MA, et al. Antimicrobials used for surgical prophylaxis by companion animal veterinarians in Australia. *Vet Microbiol*. 2017; 203:301-07.
- Holloway KA, Rosella L, Henry D. The Impact of WHO essential medicines policies on inappropriate use of antibiotics. *PLoS One*. 2016; 11(3): e0152020.
- Ierano C, Nankervis JM, James R, Rajkhowa A, Peel T, Thursky K. Surgical antimicrobial prophylaxis. *Aust Prescr*. 2017;40(6):225-29.
- Lappin MR, Blondeau J, Boothe D, Breitschwerdt EB, Guardabassi L, Lloyd DH, et al. Antimicrobial use guidelines for treatment of respiratory tract disease in dogs and cats: Antimicrobial guidelines working group of the international society for companion animal infectious diseases. *J Vet Intern Med*. 2017; 31(2): 279-94.
- Ludwig C, de Jong A, Moyaert H, El Garch F, Janes R, Klein U, et al. Antimicrobial susceptibility monitoring of dermatological bacterial pathogens isolated from diseased dogs and cats across Europe (ComPath results). *J Appl Microbio*. 2016; 121(5):1254-67.
- Michael GB, Kaspar H, Siqueira AK, de Freitas Costa E, Corbellini LG, Kadlec K, et al., Extended-spectrum  $\beta$ -lactamase (ESBL)-producing *Escherichia coli* isolates collected from diseased food-producing animals in the GERM-Vet monitoring program 2008-2014. *Veterinary Microbiology*. 2017; 200: 142-50.
- Morrissey I, Moyaert H, de Jong A, El Garch F, Klein U, Ludwig C, et al. Antimicrobial susceptibility monitoring of bacterial pathogens isolated from respiratory tract infections in dogs and cats across Europe: ComPath results. *Vet Microbiol*. 2016; 191: 44-51.
- Moyaert H, Morrissey I, de Jong A, El Garch F, Klein U, Ludwig C, et al. Antimicrobial susceptibility monitoring of bacterial pathogens isolated from urinary tract infections in dogs and cats across Europe: ComPath Results. *Microb Drug Resist*. 2017; 23(3): 391-403.
- Munita JM, Arias CA. Mechanisms of antibiotic resistance. *Microbiol Spectr*. 2016; 4(2): 1-37.
- Murphy C, Reid-Smith RJ, Prescott JF, Bonnett BN, Poppe C, Boerlin P, et al. Occurrence of antimicrobial resistant bacteria in healthy dogs and cats presented to private veterinary hospitals in southern Ontario: A preliminary study. *Can Vet J*. 2009; 50(10): 1047-53.

- Nelson R, Couto CG. Small animal internal medicine. 5<sup>th</sup> ed. St. Louis: Elsevier/Mosby publishing; 2014.
- Qekwana DN, Oguttu JW, Sithole F, Odoi A. Patterns and predictors of antimicrobial resistance among *Staphylococcus* spp. from canine clinical cases presented at a veterinary academic hospital in South Africa. BMC Vet Res. 2017; 13(1): 116-21.
- Radford AD, Noble PJ, Coyne KP, Gaskell RM, Jones PH, Bryan JG, et al. Antibacterial prescribing patterns in small animal veterinary practice identified via SAVSNET: the small animal veterinary surveillance network. Vet Rec. 2011; 169(12): 310-18.
- Rampacci E, Bottinelli M, Stefanetti V, Hyatt DR, Sgariglia E, Coletti M, et al. Antimicrobial susceptibility survey on bacterial agents of canine and feline urinary tract infections: weight of the empirical treatment. J Glob Antimicrob Resist. 2018; pii: S2213-7165(18)30013-4.
- Roopali B, Mahadappa P, Satheesha SP, Sandeep H, Kasaralikal V, Patil NA. Acute hepatozoonosis in dogs: a case report. J Parasit Dis. 2017; 41(3): 747-49.
- Schneider S, Salm F, Vincze S, Moeser A, Petruschke I, Schmäcker K, et al. Perceptions and attitudes regarding antibiotic resistance in Germany: a cross-sectoral survey amongst physicians, veterinarians, farmers and the general public. J Antimicrob Chemother. 2018; 73(7):1984-88.
- Shropshire S, Olver C, Lappin M. Characteristics of hemostasis during experimental *Ehrlichia canis* infection. J Vet Intern Med. 2018; 32(4): 1334-42.
- Tanaka N, Takizawa T, Miyamoto N, Funayama S, Tanaka R, Okano S, et al. Real world data of a veterinary teaching hospital in Japan: a pilot survey of prescribed medicines. Vet Rec Open. 2017; 4(1): e000218.
- The US Food and Drug Administration (FDA). Section 2: Active Ingredients. Green Book [Internet]. 2018. [cited 2019 Feb 8]. Available from: <https://animaldrugsatfda.fda.gov/adafda/app/search/public/ingredientsInformationPdf/Section2ActiveIngredients>.
- Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, et al. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. Lancet Infect Dis. 2014; 14(8): 742-50.
- Visschers VH, Backhans A, Collineau L, Loesken S, Nielsen EO, Postma M, et al. A Comparison of pig farmers's and veterinarians's perceptions and intentions to reduce antimicrobial usage in six European countries. Zoonoses Public Health. 2016; 63(7): 534-44.
- Weese JS, Blondeau JM, Boothe D, Breitschwerdt EB, Guardabassi L, Hillier A, et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: Antimicrobial guidelines working group of the international society for companion animal infectious diseases. Vet Med Int. 2011; 2011: 263768.
- Wilcox MH. The tide of antimicrobial resistance and selection. Int J Antimicro Agents. 2009; 34(S3): 6-10.

- Wong C, Epstein SE, Westropp JL. Antimicrobial Susceptibility patterns in urinary tract infections in dogs (2010-2013). *J Vet Intern Med.* 2015; 29(4): 1045-1052
- Wright AJ. The penicillins. *Mayo Clin Proc.* 1999; 74(3):290-307.
- Wushouer H, Zhang ZX, Wang JH, Ji P, Zhu QF, Aishan R, et al. Trends and relationship between antimicrobial resistance and antibiotic use in Xinjiang Uyghur Autonomous Region, China: Based on a 3 year surveillance data. *J Infect Public Health.* 2015; 11(3): 339-46.
- Zhuo A, Labbate M, Norris JM, Gilbert GL, Ward MP, Bajorek BV, et al. Opportunities and challenges to improving antibiotic prescribing practices through a one health approach: results of a comparative survey of doctors, dentists and veterinarians in Australia. *BMJ Open.* 2018; 8(3): e020439.