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Difficulties in administration of oral medication formulations to pet cats: an e-survey of cat owners

Sivén, M.

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1 **Original Article**

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4 **Difficulties in administration of oral medication formulations to pet cats; an e-survey of**
5 **cat owners**

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8 Mia Siven^a, PhD, Saila Savolainen^b, DVM, Sanna Ranttilä^a, MSc, Sofia Männikkö^c, MSc, Mari
9 Vainionpää^b, DVM, PhD, Sari Airaksinen^a, PhD, Marja Raekallio^b, DVM, PhD, Outi Vainio^b
10 DVM, PhD, ECVPT and Anne M Juppo^a, PhD

11
12 *^aDivision of Pharmaceutical Chemistry and Technology, Faculty of Pharmacy, University of*
13 *Helsinki, Finland*

14 *^bDepartment of Equine and Small Animal Medicine, Faculty of Veterinary Medicine,*
15 *University of Helsinki, Finland*

16 *^c4Pharma Ltd, Finland*

17
18
19 *E-mail for correspondence: mia.siven@helsinki.fi (Dr. M. Siven)*

Abstract

The purpose here was to determine the problems cat owners encounter in medicating their cats with orally administered drugs at home. The study was carried out as an open e-questionnaire survey addressed to cat owners in which we focused on the oral administration route. A total of 46 completed questionnaires were included in the survey. In the study, 46 cats received 67 orally administered drugs. Approximately half of the drugs were registered for use in cats by the European Medicines Agency (54%), and there were also off-label drugs registered for human (36%) and canine medication (7.4%) and an *ex tempore* drug (3.0%). The owners were unable to give the doses as prescribed for their cats for one fourth of the medications (16/67). Drugs that were registered for feline medication were significantly more palatable than drugs registered for other species (odds ratio (OR) 4.9), and liquid formulations were significantly more palatable than solid formulations (OR 4.8). However, most of the owners (22/38) preferred a solid dosage form, while few (4/38) chose a liquid formulation. The results indicate that there is still a need for more palatable and easily administered oral drugs for cats.

Keywords: Compliance; Dosage form; Feline; Medicine; Palatability

Introduction

Cats are popular as companion animals and are generally well cared for throughout their lifespan. Owners are willing to provide their cats with good health care and medication for illnesses on veterinarians' recommendations (Jevring, 2005). However, owners often express difficulty in medicating their pets.

Medication compliance in companion animals may be compared with that in paediatrics, since owners and parents are responsible for medicating the patient (Grave and Tanem, 1999). All medications face similar challenges, such as the patient often being reluctant to take the drug, due to unpleasant taste and a high degree of noncompliance (Matsui, 1997; Haynes et. al., 2002). In veterinary medication, owners may prefer oral solid dosage forms, such as tablets, for long-term administration because they are familiar with how to administer these dosage forms to the pet (Khor et al., 2012). A choice of palatable formulations may increase pet acceptance (Thombre, 2004). Nevertheless, the degree of compliance varies widely. In compliance studies in dogs, 27-84% of the medications were given as prescribed (Bomzon, 1978; Grave and Tanem, 1999; Adams et al., 2005). In many cases the reason for non-compliance was that the owner was unable to follow the dosing regimen, rather than the dog's resistance to medication. The owners' medication experiences, as well as animal habituation in medication, also affect compliance. Compliance is clearly a multifaceted issue, in which the owners' abilities to follow the medication instructions play an important role (AAHA, 2003). Thus, pet compliance can be evaluated indirectly through owner consumption success or as the free-choice acceptance of the drug by the pet.

Few results are available on medication compliance in cats. Cats are more difficult to medicate than dogs, due to their discriminating nature (Thombre, 2004). They can be less

accustomed to being restrained than dogs and may display fear or resistance when medicated. The free-choice acceptability in cats is typically less than 50% for conventionally flavoured tablets (Ahmed and Kasraian, 2002). Various methods for administering oral solid dosage forms to cats have been used, such as forcing the animal to swallow a tablet ('dry swallowing') by placing it in the back of the oral cavity with the fingers or by a specific device, hiding the tablet in a highly palatable food or treat, and liquefying or crushing the tablet (Thombre, 2004; Bennett et al., 2010). Consumption success has rarely been evaluated in cats. For bitter-tasting drugs, owner-estimated consumption success rates have been as high as 90% for conventional tablets (dry swallowing) and 93% for extemporaneously prepared flavoured suspensions (Khor et al., 2012). In another study, dissolving oral film strips were easier to administer than gelatin capsules (Traas et al., 2010). Dosage form palatability has been assessed in studies in association with drug efficacy evaluations (Ahmed and Kasraian, 2002; Gunew et al., 2008; Giraudel et al., 2010). In general, flavoured formulations (liquids or solids) are more palatable than conventional tablets, but comparison between studies is difficult, because various criteria for acceptance have been used. The criteria for determining palatability have been clarified quite recently by European Medicines Agency (EMA, 2014).

The aim here was to determine the difficulties cat owners encounter in administering oral medication to their pets. Information is needed for developing palatable formulations for cats, as well as the methodology for assessment of acceptance. Detailed knowledge also supports veterinarians in counselling owners. More specifically, the purpose was to evaluate the palatability of dosage forms (expressed as free-choice acceptance), ease of administration of the dosage forms and ease in following the medication schedules (owner compliance). The hypothesis was that a marked number of owners experience difficulty with one or more of these aspects in medicating their cats at home.

Materials and methods

Study outline

The study was carried out as an open e-questionnaire survey addressed to cat owners responsible for medicating their cats at home. The platform chosen was a secured online tool provided by the University of Helsinki (e-form). The term compliance was adopted, as described by Cramer et al. (2008), in which the medication compliance (synonym adherence) refers to the degree or extent of conformity to the recommendations for daily treatment by the provider with respect to the timing, dosage and frequency. The theoretical framework of the “five interacting dimensions of adherence” (Sabaté, 2003) was implemented in exploring the study aims, and the e-questionnaire was adopted within the context of veterinary medication.

The questionnaire was developed in collaboration with veterinarians and pharmacists (seven specialists, University of Helsinki). In developing the questionnaire, we focused on the five dimensions of adherence and especially on the therapy-related factors, such as the medical regimen, ease in following the regimen and ease in administration of the dosage form to the cat. Pet compliance was also evaluated as free-choice acceptance of the drug by the cat. Originally, the oral, topical, eye and ear administration routes were included, but in this study we focused on orally administered dosage forms, since it is a common route of administration. The drugs were categorized according to their target species registration; feline, canine or other (human medication or *ex tempore* drugs).

The Viikki Campus Research Ethics Committee (University of Helsinki) approved the study protocol (Statement of Approval 14.1.2010). In a pilot study, preliminary suggestions by 14 cat owners resulted in rewording of one background question and of the instructions for answering the questions. The Checklist for Reporting Results of Internet E-Surveys

(CHERRIES) (Eysenbach, 2004) was followed in reporting the results of the e-questionnaire survey.

Recruitment of cat owners

Owners who had medicated their cats were recruited from the Veterinary Teaching Hospital (University of Helsinki), four randomly chosen municipal clinics and four private veterinary clinics. One private cat clinic and the Veterinary Teaching Hospital were chosen without randomizing, due to the large numbers of their feline patients. The inclusion criteria for the cat owners was medication experience during the previous 3 months at home. The recruitment time span was 3 months.

The clinics were informed of the study via telephone calls, cover letters and e-mails. In all, 840 invitation letters were sent to the clinics that were willing to participate. The invitation letters included information on the study for the cat owners to support their decision to participate, and an Internet link to the questionnaire. The letters were distributed among the personnel of the clinics. Additionally, notices were distributed at the University Pharmacy (Viikki) and at one boarding cattery. Cat owners were also recruited from four Internet cat-themed discussion forums. One notice was posted at the University Library (Viikki). Participation in the study was voluntary, and no material incentives were provided to the participants.

Questionnaire

Demographic data on the cats and their owners were collected (Table 1). The questions concerning the dosage form and administration of the drug are described in Table 2. A total of 46 completed questionnaires on 46 cats were included in the study. Each cat

received one or more drugs; in all, 67 orally administered drugs were included (Table 3). Three completed questionnaires on orally administered drugs were excluded, one because the owner lived abroad, another because the respondent was an employee of a rescue shelter and therefore not a regular cat owner and a third because the owner did not define the drug. Another 16 completed questionnaires were excluded, because the reported administration route was not oral. The clinics were asked to return the unused invitation letters; 447/850 (53%) letters were returned.

Statistical methods

Descriptive statistics on the number of observations and percentage frequencies were presented. Statistical analyses were performed using SAS System for Windows, version 9.3 (SAS Institute Inc., Cary, NC, USA). The outcome variables concerning the owner's ability to give all the doses to the cat, free-choice acceptance of the drug, salivation, gagging or vomiting, following the medication schedule and ease in following the schedule were measured categorically, as were the explanatory variables (drug, dosage form, number of daily administrations, duration of medication, adverse effects). Frequency tables were constructed between the categories of the explanatory variables on all outcome variables. A cumulative logistic regression model was fitted to outcome variables that were evaluated through an agree-neutral-disagree-scale. The probabilities were modelled for responses having lower values (i.e. more agreement). Due to small cell frequencies, the original five-step Likert-scale (Strongly agree/Agree, Neither agree nor disagree, Disagree/ Strongly disagree) questions were transformed into three-class categorical variables, the middle class representing neutral, the lower and upper classes representing agreement and disagreement, respectively. The variable 'Number of doses administered daily' was transformed into a dichotomous variable (1 or less, more than 1). For the binary response 'Ability to give all

doses', a logistic regression model was fitted to the data, and the probability was modelled for the response value being 'yes'. All explanatory variables were analysed separately. In all models the explanatory variable in question was included in the model as the sole fixed factor. The effect of the cat was included in the model as a random effect. For all analyses, the odds ratios (ORs) and their 95% confidence intervals (CIs) were constructed to describe the group differences.

Results

Dosage form and administration schedule

Approximately half of the drugs were registered for use in cats by the EMA (Table 3). Most of these were solid dosage forms: tablets or capsules. Off-label drugs were registered for human (36%) or dog medication (7.4%) and one was an *ex tempore* tablet. All drugs were immediate-release formulations. In nearly half of the cases, the drug was used as long-term medication for chronic illnesses (Table 4). Most of the oral drugs were administered once or twice per day. However, the total administration frequency could have been higher if the cat had concurrent medications (orally administered or other routes of administration). This was the case for one third of the cats ($n = 16$). The maximum dosing requirement was five to six times per day.

When asked "*Did the cat accept the drug willingly?*", the owners agreed in 35% of the cases if the drug was registered for feline medication (Table 5). The free-choice acceptance was nearly five-fold higher (OR 4.9, $P < 0.05$) for drugs registered for cats than those registered for other species. A statistically significant relationship was also evident for the dosage form, with solutions and suspensions being more acceptable than tablets or capsules (OR 4.8). For the other questions, no statistically significant effects were observed

(Table 6). Most of the owners agreed that precisely following the medication schedule was easy.

Dosage form and administration practice

In only two cases did the cat willingly accept the drug by consuming it ‘as a treat’ (Table 7). Most of the drugs were introduced orally by dry swallowing (36/67). In addition, various methods for facilitating drug administration were described, such as mixing the drug in cat’s food or covered with a palatable treat. The cat either consumed the modified dosage form as such or else the form was introduced orally. It was also common practice for owners to first crush the tablet or dissolve it in water, after which the drug was mixed in the food or given by a syringe. If the package included an administration device, the owners found that using it was easy, and the guidance of the device was deemed adequate and clear (Table 8).

Difficulties encountered in drug treatment

No medications in which all the doses were missed were reported. However, some doses were missed in one fourth ($n = 16$) of the cases (Table 6). At most, four doses were missed for one prescribed drug ($n = 8$), and most of these cases were associated with short-term medication ($n = 6$). In general, the missed doses occurred at the beginning ($n = 6$) or in the middle ($n = 2$) of the course of medication. In response to the open question “*Why could you not give all the doses to the cat?*” ($n = 15$), most of the answers ($n = 11$) were associated with adverse effects or the individual behaviour of the cat; the cat spat the drug out ($n = 5$), vomited ($n = 2$), salivated strongly ($n = 2$) or resisted the medication ($n = 2$). For some owners, scanty medication experience made it difficult to administer the drug in the beginning ($n = 2$). Answers to the question “*Why was it difficult to follow the medication schedule?*” ($n = 15$) included adverse effects ($n = 2$) or some other feline response ($n = 2$), such as the drug

given with the food was not accepted, due to lack of appetite. One third of the responses were related to the owners' working hours ($n = 5$) or, in the case of chronic illness, it was not always possible for the owner to commit to long-term medication ($n = 2$). One owner stopped the medication, because the symptoms disappeared, but then started it again after consulting the veterinarian.

For the question, "*What was the major problem related to the drug itself or administering the drug to the cat?*", 41 out of 46 responses were obtained. One fourth of the answers concerned the bad taste of the drug ($n = 11$). Other characteristics of the dosage form were also considered problematic; these included taking the right dose by splitting the tablet ($n = 7$), the tablet size being too large ($n = 4$) or the syringe for a liquid drug being a bit difficult to use ($n = 1$). Again, the individual behaviour of the cat and adverse effects were mentioned; the cat did not willingly take the drug, and the owner had to force it ($n = 8$) or the drug caused increased salivation or other side effects ($n = 4$). However, approximately half of the owners agreed with the question "*Did the administration of the drug become easier over time?*" (Table 8).

Dosage form and administration preferences

An open question "*What kind of dosage form would you prefer in medicating your cat?*" received 38 answers (38/46). A solid dosage form was the most preferred formulation; 58% of the owners ($n = 22$) chose a tablet or capsule, while some also mentioned that the tablet should be small ($n = 8$), palatable ($n = 2$) or tasteless ($n = 1$). Four owners did not define the dosage form, only that the drug should be palatable or tasteless. Some ($n = 3$) chose either a solid or liquid formulation, if it were palatable enough, or a liquid or semisolid dosage form ($n = 4$). Few preferred injections ($n = 2$) or a pour-on formulation ($n = 1$).

The question “*What would you consider to be the easiest method for administering the drug to your cat?*” received 43 responses (43/46). Few (n = 3) answered that their cat consumed the drug willingly without any modification to the dosage form or administration aid. One third of the owners mentioned a solid dosage form by dry swallowing (n = 16). Some considered that the drug would be easiest to administer orally, but only after coating it with some palatable viscous material, such as butter (n = 4). In two cases, the owner specified that two persons would be needed to administer the drug orally. Some owners (n = 7) named liquids as the easiest dosage form; the drug should be either in a liquid form or the owner would dissolve a solid drug and then administer it orally with a syringe. For others, the easiest way was to give the drug hidden in the cat’s food or in a treat (n = 8). One owner mentioned that the cat should be hungry before medication, and one stated that the cat would lick a liquid drug from its fur. One considered injections as the easiest means of medication.

Owner counselling supported drug treatment

The owners considered themselves well informed about the medication (88%) (Table 8). In an open question, however, owners reported that they would have liked to have more information on administration methods (n=2) or how to take the right dose from the package (n=1). One owner had hoped for more information on the active pharmaceutical ingredient (drug-drug interactions, adverse effects and if the drug was sufficiently efficacious) and the presence of generic products on the market. For the question “*Did you read the drug description before administering the drug?*”, the owners agreed in 85% of the cases.

Discussion

The hypothesis was that a marked number of owners experience difficulty in

medicating their cats at home. The owners were unable to give the doses as prescribed for one fourth of the medications (24%), and therefore the owner compliance and owner consumption success can be considered to be 76%. The data indicate that off-label use of drugs is still common in the feline setting, since almost half of the drugs used were off-label. Pet compliance expressed as free-choice acceptance was higher for feline formulations than for off-label drugs, yet only in 35 % of these feline formulations did the owner agree that the cat took the drug willingly. Solutions and suspensions were significantly more acceptable than solid dosage forms. It is noteworthy that these were practically all (excluding one off-label drug) feline medications in which the palatability issues were considered in formulation development by the pharmaceutical company. In other studies, oral suspensions registered for feline medication were also well accepted by cats, either given alone or mixed in food (Litster et al., 2007; Gunew et al., 2008). Product development for feline medication is apparently progressing in the right direction, although there is further need for drugs registered specifically for cats, based on the amount of off-label usage.

Most consumption failures were related to the individual behaviour of the cat (the cat resisted the medication or spat the drug out) or adverse effects (such as strong salivation). Some failures may have been caused by the bad taste of the drug, which the owners presented as an important reason. Interestingly, the owners preferred tablets as a dosage form, although there was significantly better pet compliance with the liquids. In most cases, tablets were administered orally 'dry swallowing'. Such preference may be explained by the owner being familiar with the administration technique (Khor et al., 2012). The 'dry swallowing' method applies when medicating cats with a compliant nature, but is problematic in cases in which the cat shows fear or resistance. In forcing, the cat may become even more unwilling to take the drug, which may negatively affect both the human animal relationship and owner

compliance. The safety of the person administering the medicine should also be considered (Bennett et al., 2010). An alternative approach to support pet compliance could be training the pet to be more favourable to handling and drug administration already as a kitten. In medicating cats with chronic illnesses, maintaining compliance is crucial (Jevring, 2005). In our data, nearly half of the medications were long-term.

Administration practice varied markedly and owners described several methods for avoiding consumption failure. The tablets may have been easier to handle than liquid dosage forms, because they (if small enough) could be given inside a treat or with other palatable material. Nevertheless, it is known that solid dosage forms given by dry swallowing can become trapped in the oesophagus and cause esophagitis or even stricture formation (German et al., 2005; Beatty et al., 2006). Therefore, several authors have recommended that solid oral dosage forms should be given with a water bolus or a small amount of food to facilitate oesophageal clearance, or otherwise with an administration aid such as a pill delivery treat or flavoured liquid (Graham et al, 2000; Westfall et al., 2001; Bennett et al., 2010). Furthermore, owners facilitated administration by giving the drug mixed in the cat's food. The food approach may, however, be problematic, because the food effects on bioavailability of the drug substance or the dosage form performance may not be easily managed (Ahmed and Kasraian, 2002).

Our results suggest that the free-choice acceptance and ease of dosage form administration are still problematic in feline medication. This often seems to be related to the use of off-label drugs. Thus, there is need for pharmaceutical development of solid dosage forms for cats in particular. Species-specific considerations are needed, including tablet size and formulations that enhance free-choice acceptance and ease in swallowing. Dosage form

characteristics, including small tablet size, palatability or tastelessness were preferred by cat owners in the present study.

One limitation of the study was the relatively small sample size. Information on a total of 46 cats and 67 orally administered drugs was provided in the study. The low survey response rate made the study subject to non-response bias, and the results may have led to overestimation of the owners' compliance and abilities to medicate the cat, using oral medication formulations. The more compliant owners were more likely to have been respondents. As an open e-questionnaire, the survey relied on a convenience sample, which may have led to undercoverage of noncompliant owners or owners who have limited access to the Internet. The retrospective study setting increased the risk for pet owner recall bias for self-reported data.

Conclusion

Our results confirm that there is need for developing new palatable and easily administered drugs for feline medication. Medications registered for feline administration were more palatable than off-label drugs, even though the owners reported that their cats took the drugs willingly in only 35 % of these cases. To improve the willingness of cats to ingest the drugs, as well as owner compliance, the individual nature of the cat should be taken into account, and not only effective, but also easily administrable dosage forms should be developed for cats.

References

- AAHA (American Animal Hospital Association) (2003) AAHA study finds millions of pets aren't getting maximum health care. *Journal of the American Veterinary Medical Association* 222, 1488-1488
- Adams, V.J., Campbell, J.R., Waldner, C.L., Dowling, P.M., Shmon, C.L. (2005) Evaluation of client compliance with short-term administration of antimicrobials to dogs. *Journal of the American Veterinary Medical Association* 226, 567-574
- Ahmed, I., Kasraian, K. (2002) Pharmaceutical challenges in veterinary product development *Advanced Drug Delivery Reviews* 54, 871
- Beatty, J.A., Swift, N., Foster, D.J., Barris, V.R. (2006) Suspected clindamycin-associated oesophageal injury in cats: five cases. *Journal of Feline Medicine and Surgery* 8, 412-419
- Bennett, A.D., MacPhail, C.M., Gibbons, D.S., Lappin, M.R. (2010) A comparative study evaluating the esophageal transit time of eight healthy cats when pill with the FlavoRx pill glide versus pill delivery treats. *Journal of Feline Medicine and Surgery* 12, 286-290
- Bomzon, L. (1978) Short-term antimicrobial therapy - A pilot compliance study using ampicillin in dogs. *Journal of Small Animal Practice* 19, 697-700
- Cramer, J.A., Roy, A., Burrell, A., Fairchild, C.J., Fuldeore, M.J., Ollendorf, D.A., Wong, P.K. (2008) Medication Compliance and Persistence: Terminology and Definitions. *Value in Health* 11, 44-47
- EMA (European Medicines Agency) (2014) Guideline on the demonstration of palatability of veterinary medicinal products. EMA/CVMP/EWP/206024/2011
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/07/WC500170030.pdf (Accessed 27th June 2016)
- Eysenbach, G. (2004) Improving the Quality of Web Surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *Journal of Medicinal Internet Research* 6(3), e34
- German, A.J., Cannon, M.J., Dye, C., Booth, M.J., Pearson, G.R., Reay, C.A., Gruffyd-Jones, T.J. (2005) Oesophageal strictures in cats associated with doxycycline therapy. *Journal of Feline Medicine and Surgery* 7, 33-41
- Giraudel, J.M., Gruet, P., Alexander, D.G., Seewald, W., King, J.N. (2010) Evaluation of orally administered robenacoxib versus ketoprofen for treatment of acute pain and inflammation associated with musculoskeletal disorders in cats. *American Journal of Veterinary Research* 71, 710-719
- Graham, J.P., Lipman, A.H., Newell, S.M., Roberts, G.D. (2000) Esophageal transit of capsules in clinically normal cats. *American Journal of Veterinary Research* 61, 655-657
- Grave, K., Tanem, H. (1999) Compliance with short-term oral antibacterial drug treatment in dogs. *Journal of Small Animal Practice* 40, 158-162
- Gunew, M.N., Menrath, V.H., Marshall, R.D. (2008) Long-term safety, efficacy and palatability of oral meloxicam at 0.01-0.03 mg/kg for treatment of osteoarthritic pain in cats.

- 373 *Journal of Feline Medicine and Surgery* 10, 235-241
- 374 Haynes, R.B., McDonald, H.P., Garg, A.X. (2002) Helping patients follow prescribed
375 treatment: clinical applications. *Journal of the American Medical Association* 288, 2880-2883
- 376 Jevring, C. (2005) Compliance in veterinary practice. *European Journal of Companion*
377 *Animal Practice* 15, 205-209
- 378 Khor, K.H., Campbell, F., Rathbone, M.J., Greer, R.M., Mills, P.C. (2012) Acceptability and
379 compliance of atenolol tablet, compounded paste and compounded suspension prescribed to
380 healthy cats. *Journal of Feline Medicine and Surgery* 14, 99-106
- 381 Litster, A., Moss, S., Honnery, M., Rees, B., Edingloh, M., Trott, D. (2007) Clinical efficacy
382 and palatability of pradofloxacin 2.5% oral suspension for the treatment of bacterial lower
383 urinary tract infections in cats. *Journal of Veterinary Internal Medicine* 21, 990-995
- 384 Matsui, D.M.S. (1997) Drug compliance in pediatrics. *Pediatric Clinics of North America* 44,
385 1-14
- 386 Sabaté, E. Editor (2003) Adherence to long term therapies: Evidence for action. Section II:
387 Improving adherence rates: Guidance for countries, Chapter V, 27-30. World Health
388 Organization. www.who.int/chp/knowledge/publications/adherence_full_report.pdf (Accessed
389 30th June 2016)
- 390 Thombre, A.G. (2004) Oral delivery of medications to companion animals: Palatability
391 considerations. *Advanced Drug Delivery Review* 56, 1399-1413
- 392 Traas, A.M., Fleck, T., Ellings, A., Mahabir, S., Stuebner, K., Brown, D.C., Durso, D.,
393 DiGregorio, M., Bode, L., Kievit, K.I., McCall, R. (2010) Ease of oral administration and
394 owner-perceived acceptability of triglyceride oil, dissolving thin film strip, and gelatin
395 capsule formulations to healthy cats. *American Journal of Veterinary Research* 71, 610-614
- 396 Westfall, D.S., Twedt, D.C., Steyn, P.F., Oberhauser, E.B., VanCleave, J.W. (2001)
397 Evaluation of esophageal transit of tablets and capsules in 30 cats. *Journal of Veterinary*
398 *Internal Medicine* 15, 467-470

TABLES

Table 1. Demographic data on cats and their owners (a total of 67 oral medications in 46 cats).

Pedigree cats	25 (54%)
Domestic cats ^a	21 (46%)
Age of the cat (years)	0.25 to 17 years (average 7.1 years, SD $\pm$ 5.1)
Castrated males	23 (50%)
Spayed females	13 (28%)
Intact males	6 (13%)
Intact females	4 (9%)
Number of cats in household	median 2.5 (average 3.6, SD $\pm$ 2.8, range 1 to 12 cats)
Persons responsible for medicating the cat ^b	
One	28 (61%)
Two	17 (37%)
Three	1 (2%)
All owners reported previous experience in medicating cats (the level of experience was not rated)	

^a Short hair or long hair domestic cat^b One of which was the owner

Table 2. Questions concerning the dosage form and administration of medication to the cat. The type of question is indicated by the letters a, b, c and d.

Specify the dosage form administered to the cat *
How many doses were administered daily? a
How many drugs were administered concurrently? a
If the cat had concurrent medications, what was the total daily administration frequency? a
What was the duration of drug treatment? b
How was the drug given to the cat? b **
Did you use some kind of administration aid in giving the drug to the cat? b ***
Did the cat accept the drug willingly? c
Did the salivation of the cat increase while giving the drug? c
Did the cat begin to gag or vomit during ingestion of the drug? c
Did the drug cause any adverse effects? Which adverse effects? b ****
Was it easy to follow the medication schedule? c
Did you follow the medication schedule precisely? c
Why was it difficult to follow the medication schedule? d
Was it easy to provide a single dose from the package? c
Was the guidance of the administration device provided in the package adequate and clear? c
Was the use of the administration device easy? c
Did the administration of the drug become easier over time? c
Were you able to give all the doses? c
How many doses were missed? d
When were the doses missed? d
Why could you not give all the doses to the cat? d
What was the major problem related to the drug itself or administering the drug to the cat? d
What kind of dosage form would you prefer in medicating your cat? d
What would you consider to be the easiest method for administering the drug to your cat? d
Did you read the drug description before administering the drug? c
Did you receive enough information about the correct use of the drug? c
What kind of information would you have liked to have more of? d

a Numeric field

b Multiple choice question

c Likert scale (Strongly agree/Agree, Neither agree nor disagree, Disagree/Strongly disagree)

d Open question

* The drug was picked from a list of names and images of 50 commonly used drugs registered for feline medication in the European Medicines Agency (EMA). If the drug was not on the list, it was reported in open question.

** Orally (“dry swallowing”), from a cat’s food bowl mixed with food, inside a treat, crushed, dissolved, other (please describe how), cat refuses to take the medication

*** Inside a treat, with palatable viscous paste, pill gun, dispensed in a gelatin capsule, other administration aid (please describe which?), no administration aid was used

**** Diarrhoea, constipation, nausea, dizziness and/or fatigue, skin symptoms other side effects, (please describe which)

Adoptive questioning was used; where appropriate the question was conditionally displayed, based on response to the previous question. Review of the answers by the respondents (back button) and completeness check by the system for mandatory items (highlighted) were enabled before the questionnaire was submitted.

Table 3. Frequency of different types of oral dosage forms (a total of 67 medications in 46 cats).

	Tablet/ capsule	Solution/ suspension	Total
	n	n	n (%)
Registered for cats	25 ^a	11 ^b	36 (54)
Registered for dogs	5 ^c	0	5 (7)
Drugs for human medication (off-label drugs)	23 ^d	1 ^e	24 (36)
<i>Ex tempore</i> drugs	2 ^f	0	2 (3)
Total n (%)	55 (82%)	12 (18%)	67 (100)

^a Axilur 250 mg or 500 mg tabl., Clavubactin 50/12,5 mg or 250/62,5 mg tabl., Drontal 230/20 mg tabl., Fortekor 2,5 mg or 5 mg tabl., Medrol vet 4 mg tabl., Perlutex vet 5 mg tabl., Synulox 40 mg, 200 mg or 400 mg tabl., Xeden 15 mg or 50 mg tabl.

^b Amovet 50 mg/mL susp., Metacam 0,5 mg/mL susp., Flubenol 44 mg/mL paste, Mirrix 11,5% paste

^c Atopica 25 mg tabl., Barbivet 30 mg tabl., Cerenia 16 mg tabl., Furovet 20 mg tabl., Metacam 1 mg tabl.,

^d Anafranil 10 mg tabl., Atarax 25 mg tabl., Clinaxin 75 mg caps., Dexametason 1,5 mg tabl., Dilzem 30 mg tabl., Disperin 50 mg tabl., Doximycin 100 mg tabl., Norvasc 5 mg tabl., Pepcid 10 mg tabl., Prednisolon 5 mg tabl., Tenobloc 25 mg tabl., Trikozol 200 mg tabl., Tyrazol 5 mg tabl.

^e Primperan 1mg/mL sol.

^f Tylosin tabl. (University Pharmacy)

Table 4. Administration frequency of oral dosage forms and duration of the treatment (a total of 67 medications in 46 cats). Number of concurrently administered medications (orally administered and other routes of administration, if any) and subsequent administration frequency for the cat (n = 46).

	One n (%)	Two n (%)	Three or more n (%)	Less than one n (%)
Administration times per day for one medication	30 (45)	33 (49)	1 (1.5)	3 (4.5)
Medications for one cat	30 (65)	13 (28)	3 (7)	0
Total administration times per day for one cat	17 (37)	17 (37)	10 (22) ^a	2 (4)
Duration of drug treatment				
Short term (10 days or less)				
Long term (more than 10 days)	38 (57)			
	29 (43)			

^a Four, three, one and two cats were medicated three, four, five and six times per a day, respectively

Table 5. Drug and dosage form as explanations for the question “Did the cat accept the drug willingly?” (a total of 67 medications in 46 cats).

		NA	Agree	Neither agree nor disagree	Disagree
		n	n (%)	n (%)	n (%)
Drug ^a	Registered for cats	2	12 (35.3)	4 (11.8)	18 (52.9)
	Registered for dogs	0	1 (20.0)	0	4 (80.0)
	Other	2	2 (8.3)	2 (8.3)	20 (83.3)
	Total	4	15 (23.8)	6 (9.5)	42 (66.7)
Drug formulation ^b	Tablet/capsule	4	9 (17.6)	5 (9.8)	37 (72.5)
	Solution/suspension	0	6 (50.0)	1 (8.3)	5 (41.7)
	Total	4	15 (23.8)	6 (9.5)	42 (66.7)

NA = Not answered

^a Statistically significant ($P < 0.05$) when drug registered for cats was compared with other drugs, odds ratio OR (95% confidence interval CI) 4.947 (1.086 – 22.525).

^b Statistically significant ($P < 0.05$) when solution/suspension was compared with tablet/capsule, OR (95% CI) 4.776 (1.072 – 21.274).

Table 6. Other questions concerning the dosage form and administration schedule (a total of 67 medications in 46 cats).

	NA	Agree	Neither agree nor disagree	Disagree
	n	n (%)	n (%)	n (%)
Was the owner able to give all the doses?	0	51 (76.1)	0	16 (23.9)
Did the salivation of the cat increase while giving the drug?	4	22 (34.9)	7 (11.1)	34 (54.0)
Did the cat begin to gag or vomit during ingestion of the drug?	7	12 (20.0)	3 (5.0)	45 (75)
Was it easy to follow the medication schedule?	0	58 (86.6)	2 (3.0)	7 (10.4)
Did the owner follow the medication schedule precisely?	0	53 (79.1)	7 (10.4.)	7 (10.4)

NA = Not answered. No statistically significant effects were found when the drug, dosage form, daily administration times, duration of the medication and adverse effects were tested as explanations for the question.

Table 7. Questions concerning administration practice (a total of 67 medications in 46 cats).

	Dry swallowing	Mixed with food in a bowl	Inside a treat ^b	Crushed or dissolved ^c	Other ^d
How was the drug given to the cat? ^a	36	8	11	13	15
Did you use some kind of administration aid in giving the drug to the cat?	No aid		Inside a treat (9) Palatable viscous paste (2)		Pill gun (1) Syringe (9) Gelatin capsule (2) Spoon (1)

^a Multiple responses possible, ^b inside a treat or the tablet was covered with Easypill® or butter, ^c crushed and then mixed with food (n = 5), dissolved in water and then mixed with food or given with syringe (n = 8), ^d other: some kind of administration aid was used (n = 13), in two cases the drug was consumed as a treat. No answers were obtained for the category “cat refuses to take the medication”.

Table 8. Other questions concerning administration practice and administration device (a total of 67 medications in 46 cats).

	NA	Agree	Neither agree nor disagree	Disagree
	n	n (%)	n (%)	n (%)
Was it easy to provide a correct single dose from the package?	0	49 (73.1)	1 (1.5)	17 (25.4)
Was the guidance of the administration device adequate and clear? ^a	0	39 (58.2)	24 (35.8)	4 (6.0)
Was the use of the administration device easy? ^a	0	32 (47.8)	31 (46.2)	4 (6.0)
Did the administration of the drug become easier over time?	0	35 (52.2)	12 (17.9)	20 (29.9)
Did you read the drug description before administering the drug?	0	57 (85.0)	2 (3.0)	8 (12.0)
Did you receive enough information about the correct use of the drug?	0	59 (88.0)	4 (6.0)	4 (6.0)

NA = Not answered

^a Administration device provided in the drug package was related to solution/suspension formulations (n = 12)