doi.org/10.3406/bavf.2026.71194

Successful management of a clinical case of feline trichomonosis: combining tinidazole therapy and probiotics

Gestion réussie d'un cas clinique de trichomonose féline : combinaison d'un traitement au tinidazole et de probiotiques

Mohamed Mammeri[1], *Noelle Cochet-Faivre*[2], *Matthias Kohlhauer*[3], *Bruno Polack*[4]

Manuscrit initial reçu le 14 mai 2026, manuscrit révisé reçu et accepté le 31 mai 2026, révision éditoriale le 30 juin 2026.

ABSTRACT

Feline trichomonosis, caused by *Tritrichomonas foetus* (syn. *Tritrichomonas blagburni*), is a frequent cause of chronic large bowel diarrhea in young cats living in multi-cat environments. Diagnosis primarily relies on fecal PCR, as microscopy or culture may miss asymptomatic carriers that contribute to transmission in breeding facilities and shelters. An 11-month-old neutered male Toyger cat presented with a 5-month history of recurrent diarrhea with mucus and fresh blood. Routine fecal examinations and *Giardia duodenalis* testing were negative, but quantitative PCR confirmed a high burden of *T. foetus*. Due to the unavailability of ronidazole, the cat was treated with gastro-resistant capsules containing tinidazole (30 mg/kg/day) orally for three weeks, combined with a multi-strain probiotic formulation (Vivomixx® 112) for four weeks. Initial transient worsening of diarrhea was observed, but clinical improvement became evident after 14 days, with normalization of stool consistency and progressive weight gain. No neurological or systemic adverse effects were reported. Follow-up PCR testing one week and six months after treatment remained negative, confirming sustained parasitological clearance. This case supports tinidazole as a potential therapeutic option and emphasizes the importance of systematic PCR monitoring in cattery settings. Importantly, the combined antiparasitic and probiotic approach may improve digestive comfort, reduce recurrence risk, and represent a safe, innovative complementary protocol requiring further clinical investigation.

Keywords: feline trichomonosis, *Tritrichomonas fœtus*, tinidazole, probiotic

1- Anses, INRAE, École Nationale Vétérinaire d'Alfort, UMR BIPAR, Laboratoire de Santé Animale, 94700, Maisons-Alfort, France, courriel : mohamed.mammeri@vet-alfort.fr
2- Anses, INRAE, École Nationale Vétérinaire d'Alfort, UMR BIPAR, Laboratoire de Santé Animale, 94700, Maisons-Alfort, France, courriel : noelle.cochet-faivre@vet-alfort.fr
3- École Nationale Vétérinaire d'Alfort, IMRB, F-94700 Maisons-Alfort, France, courriel : matthias.kohlhauer@vet-alfort.fr
4- Anses, INRAE, École Nationale Vétérinaire d'Alfort, UMR BIPAR, Laboratoire de Santé Animale, 94700, Maisons-Alfort, France, courriel : bruno.polack@vet-alfort.fr,

Bull. Acad. Vét. France — 2026
https://academie-veterinaire.fr

RÉSUMÉ

La trichomonose féline, causée par Tritrichomonas fœtus *(syn.* Tritrichomonas blagburni*), constitue une cause fréquente de diarrhée chronique du gros intestin chez les jeunes chats vivant en collectivités félines. Le diagnostic repose principalement sur la PCR fécale, car les examens microscopiques ou les cultures peuvent ne pas détecter les porteurs asymptomatiques participant à la transmission au sein des élevages et des refuges. Un chat mâle Toyger castré, âgé de 11 mois, a été présenté pour une diarrhée récidivante évoluant depuis cinq mois, associée à du mucus et du sang frais. Les examens coprologiques de routine, ainsi que la recherche de Giardia duodenalis, se sont révélés négatifs, tandis qu'une PCR quantitative a confirmé une forte charge de* T. fœtus*. En raison de l'indisponibilité du ronidazole, l'animal a été traité avec du tinidazole sous forme de gélules gastro-résistantes (30 mg/kg/jour), administrées par voie orale pendant trois semaines, associé à un probiotique multi-souches (Vivomixx® 112) durant quatre semaines. Une aggravation transitoire initiale de la diarrhée a été observée, mais une amélioration clinique est devenue évidente au bout de 14 jours, avec une normalisation progressive de la consistance des selles et une reprise pondérale. Aucun effet indésirable neurologique ou systémique n'a été rapporté. Les contrôles par PCR réalisés une semaine, puis six mois après la fin du traitement sont restés négatifs, confirmant une élimination parasitologique durable. Ce cas suggère que le tinidazole pourrait constituer une alternative thérapeutique potentielle et souligne l'importance d'un suivi systématique par PCR dans les élevages félins. L'association de probiotiques au traitement antiparasitaire pourrait améliorer le confort digestif, réduire le risque de récidive et constituer une approche complémentaire innovante et sûre, méritant des investigations cliniques supplémentaires.*

Mots-clés *: trichomonose féline,* Tritrichomonas fœtus*, tinidazole, probiotique.*

Citation

Mammeri M, Cochet-Faivre N, Kohlhauer M, Polac B (2026) Successful management of a clinical case of feline trichomonosis: combining tinidazole therapy and probiotics [*Gestion réussie d'un cas clinique de trichomonose féline : combinaison d'un traitement au tinidazole et de probiotiques*] *Bulletin de l'Académie vétérinaire de France* 179: 71194. https://doi.org/10.3406/bavf.2026.71194

Introduction

Feline trichomonosis, caused by *Tritrichomonas foetus* (syn. *Tritrichomonas blagburni*), is a common large-intestine disorder in cats and a frequent cause of chronic, recurrent diarrhea, often accompanied by mucus and fresh blood (Bastos *et al.*, 2019; Gookin *et al.*, 1999, 2017). Resolution tends to be prolonged in group-housing environments, after dietary changes, or following paromomycin treatment (Foster *et al.*, 2004). Diagnosis most commonly relies on detecting trophozoites via fecal PCR assays or by microscopic examination or culture of fresh feces. However, microscopy and culture may fail to detect clinically healthy asymptomatic carriers, who are an important source of infection in multi-cat settings, such as breeding colonies or shelters (Gookin *et al.*, 2003, 2004). This cosmopolitan disease is a frequent reason for veterinary consultation, particularly in cats under one year of age originating from such environments. Treatment most often involves ronidazole, an off-label drug in cats associated with a risk of neurotoxicity (Gookin *et al.*, 2006). Oral administration at 30 mg/kg/day for 14 days has been recommended as the most effective regimen despite these concerns (Gruffydd-Jones *et al.*, 2013). At higher doses (≥60 mg/kg/day for 14 days), neurotoxic signs may develop within 3–9 days, including anorexia, weakness, altered consciousness, tremors, ataxia, and hyperaesthesia (Rosado *et al.*, 2007). These adverse effects are related to rapid systemic absorption, high bioavailability, and slow elimination (LeVine *et al.*, 2011). Ronidazole has been unavailable in France for more than a year due to stock shortages. The European Advisory Board on Cat Diseases (ABCD) Guidelines recommend tinidazole, a 5-nitroimidazole derivative antimicrobial used off-label in cats, at 30 mg/kg orally once daily for 14 days. This recommendation is based on an experimental study showing that tinidazole reduced parasite shedding and detection *in vivo*, with clinical improvement in some cats and no major adverse effects, although complete clearance was not consistently achieved (Gookin *et al.*, 2007). Relapses have been reported 6–8 weeks after treatment, particularly following amoxicillin administration. Given the parasite's dependence on the host bacterial microbiota, antibiotic-induced dysbiosis may exacerbate disease and prolong recovery. Therefore, intestinal dysbiosis associated with trichomonosis (Sui *et al.*, 2024) and antimicrobial therapy (Foster *et al.*, 2004) highlight the potential benefit of probiotics in restoring microbiota balance, reducing colonic inflammation, and limiting recurrence. In this context, combining tinidazole with probiotic supplementation may represent a safer, innovative complementary strategy that integrates antiparasitic activity with microbiome support to optimize digestive comfort and clinical outcomes. The main objective of this case report was to assess the clinical and parasitological efficacy of tinidazole combined with a probiotic in the treatment of feline trichomonosis.

Case Description

An 11-month-old neutered male Toyger cat presented with a 5-month history of chronic diarrhea, intermittently accompanied by mucus and fresh blood. The cat lived in a breeding facility with multiple cats (n=10), none of which showed clinical signs of trichomonosis. Coproscopic examinations were performed (Parasitology Laboratory, Biopôle Alfort, École nationale vétérinaire d'Alfort, France) and did not reveal any other parasitic infection. In addition, an immunofluorescence assay for the detection of *Giardia duodenalis* (Mammeri et *al.*, 2018) was carried out, with no cysts identified in the feces. Subsequently, a fecal quantitative PCR targeting *T. fœtus* was performed (Zoolyx, Belgium) and returned a positive result, with a high parasite burden (Ct = 19; positive threshold Ct ≤40). A fecal scoring system was used to monitor clinical improvement: 1 = liquid/diarrheic; 2 = soft, poorly formed; 3 = well formed, ideal texture; 4 = firm, slightly dry; 5 = very hard, dry pellets (Royal Canin, 2025).

Prognosis, Therapeutic Management and Follow-Up

Due to the unavailability of ronidazole, treatment was initiated using size 3 transparent, chicken-flavored, gastro-resistant capsules containing tinidazole (Fasygin® 500 mg, human formulation). Tinidazole was administered off-label at 30 mg/kg/day orally for 3 weeks. Similar to ronidazole, tinidazole use in cats remains off-label and was therefore administered under veterinary supervision in this clinical case. In parallel, one oral capsule of Vivomixx® 112 (112 × 10 CFU[2] of multiple bacterial strains; Visbiome®, DeSimone Formulation®; Danisco-DuPont, Madison, WI, USA) was administered daily, starting at the beginning of therapy and continuing for 4 weeks. Thus, probiotic supplementation was maintained for one additional week after completion of tinidazole treatment. At the end of the probiotic course, a follow-up PCR was performed one week after stopping tinidazole, enabling the breeder to undertake therapeutic monitoring through a scheduled post-treatment appointment. At treatment onset, the cat weighed 4.90 kg and gradually gained weight throughout the treatment course. By the end of tinidazole therapy (3 weeks), body weight had increased to 5.55 kg, representing a gain of 0.65 kg within one month. The cat's overall condition improved during and after treatment, with no signs of anorexia, lethargy, or neurotoxicity. However, during the first six days of therapy, fecal incontinence and more severe diarrhea were noted (score = 1) (**Figure 1**). By day 7, incontinence had resolved, and defecation frequency decreased. After 14 days, marked improvement was observed, with stool consistency reaching a fecal score of 3. Appetite returned at this stage. A brief episode of diarrhea lasted 2 days, beginning one day after completion of tinidazole, but stools normalized again (score = 3) by the end of probiotic supplementation. No further diarrhea was reported thereafter. Fecal quantitative PCR targeting *T. fœtus* (Zoolyx, Belgium) was performed at one week and six months after treatment completion and remained negative.

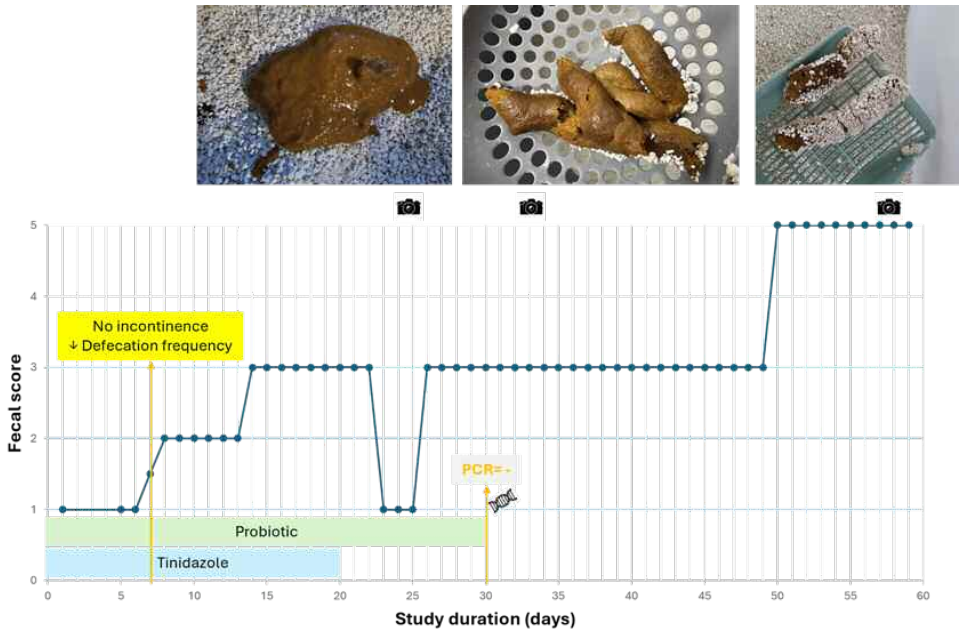

Figure 1. *Daily fecal score (Royal Canin 2025) during the treatment period in a naturally infected cat. Camera icons indicate the days when photos of the cat feces were taken (days 24, 33, and 58).*
1 = liquid/diarrheic; 2 = soft, poorly formed; 3 = well formed, ideal texture; 4 = firm, slightly dry; 5 = very hard, dry pellets.

2- CFU: colony forming unit

Discussion

In this clinical case, we report the successful eradication of *T. fœtus* and an improvement in digestive clinical signs in a cat following a combination treatment consisting of off-label oral tinidazole for 3 weeks and a probiotic (Vivomixx® 112). Tinidazole has previously been shown to be effective both *in vitro* and *in vivo*; however, due to the persistence of diarrhea and the occurrence of reinfestation, it has been considered ineffective (Gookin *et al.*, 2007; Pennisi *et al.*, 2012). These studies did not specifically recommend probiotic supplementation to address the dysbiosis associated with trichomonosis and only recommended a 2-week tinidazole treatment course. Therefore, the addition of a probiotic was considered potentially beneficial in aiding the restoration of a balanced gut microbiome. We examined supplementation with Vivomixx® 112, a well-tolerated probiotic, including in human medicine, making it a promising supportive strategy (Baldassarre *et al.*, 2018). This combined probiotic—tinidazole approach to digestive clinical signs is consistent with outcomes reported in a human study, in which adding *Lactobacillus reuteri* to *Helicobacter pylori* treatment in children reduced antibiotic-related gastrointestinal side effects, including those associated with tinidazole (Lionetti *et al.*, 2006). The potential role of *Lactobacillus*-containing probiotics should also be emphasized when interpreting the present case. Vivomixx® contains several *Lactobacillus* species known for their beneficial effects on intestinal homeostasis, including modulation of the gut microbiota, enhancement of mucosal barrier function, and reduction of intestinal inflammation. In feline trichomonosis, where intestinal dysbiosis appears to play an important role in disease persistence and severity, supplementation with *Lactobacillus*-based probiotics may therefore contribute to restoration of microbial balance and to improvement of digestive function. In addition, several studies in veterinary and comparative medicine have suggested that *Lactobacillus* spp. may reduce gastrointestinal adverse effects associated with antimicrobial therapies and promote recovery of normal fecal consistency (Lionetti *et al.*, 2006; Sivamaruthi *et al.*, 2025; Stokes *et al.*, 2017). Although the precise contribution of probiotics cannot be isolated in this single case, the favorable clinical evolution observed after the combined administration of tinidazole and Vivomixx® supports the hypothesis that microbiome-targeted supportive therapy could represent a valuable adjunctive approach in the management of feline trichomonosis.

In unwell kittens, particularly when parasitic status is unknown or giardiasis has been identified, metronidazole prescription is generally avoided to prevent potential cross-resistance with ronidazole, the principal trichomonosis treatment. Co-infections of *Giardia duodenalis* and *T. foetus* are not uncommon in cats, with reported prevalence ranging from 4.35% to 22.72% (Kingsbury *et al.*, 2010; Kuehner *et al.*, 2011; Zanzani *et al.*, 2016). Thus, the therapeutic protocol described here could also be applied in cases of co-infection, as tinidazole (30 mg/kg/day orally for 14 days) has proven effective in treating mixed trichomonosis—giardiasis infections in cats infected with feline immunodeficiency virus (FIV) (Pennisi *et al.*, 2012). Nevertheless, further investigation of tinidazole pharmacokinetics in cats is needed to establish precise dosing recommendations, explore the possibility of less frequent administration schedules, and assess the optimal treatment duration. Additionally, optimizing formulations, such as guar gum—based delivery systems that release the active compound directly in the colon through bacterial activity, may enhance therapeutic efficacy and shorten treatment duration. It is also important to note that even without treatment, diarrhea may resolve spontaneously within two years as an effective immune response develops (Foster *et al.*, 2004). Nevertheless, in the present case, the marked clinical signs observed before treatment initiation and the rapid improvement in the diarrhea score following administration of tinidazole combined with probiotics strongly support a therapeutic effect. This study also underscores the importance of systematic quantitative PCR testing for both definitive diagnosis and epidemiological surveillance in cattery settings, where asymptomatic carriers may contribute silently to parasite persistence and transmission. Consequently, group-level screening and post-therapeutic monitoring should be strongly considered, even in the absence of clinical signs, to improve infection control and reduce the risk of recurrence within multi-cat environments. Clinical evolution did not strictly parallel parasitological status, emphasizing the value of follow-up PCR assays. Tinidazole may represent a potential therapeutic alternative, provided that careful monitoring for neurological toxicity is implemented. Long-term surveillance remains essential, and adjunctive probiotic supplementation may help shorten recovery time. This case report suggests the need for long-term, large-scale, and multi-center clinical trials to assess the efficacy of the new approach.

Conclusion

The combination of tinidazole and probiotics showed promising clinical outcomes in feline trichomonosis, suggesting a potential benefit in addressing both infection and associated dysbiosis. This protocol may be particularly relevant in co-infections and cattery settings, where PCR monitoring and group-level management are essential. However, further studies on tinidazole pharmacokinetics, optimized formulations, and long-term safety are needed. Adjunctive probiotic supplementation could represent a valuable supportive strategy to enhance recovery and reduce treatment-related adverse effects.

Ethical Approval

The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards ("best practice") of veterinary clinical care for the individual patient were always followed. Ethical approval from a committee was therefore not specifically required for publication.

Informed Consent

Informed consent was obtained from the owner or legal custodian of all animal(s) described in this work. No animals or people are identifiable within this publication, and therefore, additional informed consent for publication was not required.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, or publication of this article.

Acknowledgments

The authors would like to thank the cat's owners for their valuable contribution to the description of this case, and Dr. Rachel Peat for her diligent proofreading of the manuscript.

References

• Baldassarre, M. E., Di Mauro, A., Tafuri, S., Rizzo, V., Gallone, M. S., Mastromarino, P., Capobianco, D., Laghi, L., Zhu, C., Capozza, M., & Laforgia, N. (2018). Effectiveness and Safety of a Probiotic-Mixture for the Treatment of Infantile Colic: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial with Fecal Real-Time PCR and NMR-Based Metabolomics Analysis. *Nutrients*, 10(2), 195. https://doi.org/10.3390/nu10020195

• Bastos, B. F., Almeida, F. M. de, & Brener, B. (2019). What is known about *Tritrichomonas foetus infection in cats? Revista Brasileira De Parasitologia Veterinaria = Brazilian Journal of Veterinary Parasitology: Orgao Oficial Do Colegio Brasileiro De Parasitologia Veterinaria*, 28(1), 1 11. https://doi.org/10.1590/S1984-29612019005

• Foster, D. M., Gookin, J. L., Poore, M. F., Stebbins, M. E., & Levy, M. G. (2004). Outcome of cats with diarrhea and *Tritrichomonas foetus infection*. *Journal of the American Veterinary Medical Association*, 225(6), 888 892. https://doi.org/10.2460/javma.2004.225.888

• Gookin, J. L., Breitschwerdt, E. B., Levy, M. G., Gager, R. B., & Benrud, J. G. (1999). Diarrhea associated with trichomonosis in cats. *Journal of the American Veterinary Medical Association*, 215(10), 1450 1454.

• Gookin, J. L., Copple, C. N., Papich, M. G., Poore, M. F., Stauffer, S. H., Birkenheuer, A. J., Twedt, D. C., & Levy, M. G. (2006). Efficacy of ronidazole for treatment of feline *Tritrichomonas foetus infection*. *Journal of Veterinary Internal Medicine*, 20(3), 536 543. https://doi.org/10.1892/0891-6640(2006)20[536:eorfto]2.0.co;2

• Gookin, J. L., Foster, D. M., Poore, M. F., Stebbins, M. E., & Levy, M. G. (2003). Use of a commercially available culture system for diagnosis of *Tritrichomonas foetus infection in cats*. *Journal of the American Veterinary Medical Association*, 222(10), 1376 1379. https://doi.org/10.2460/javma.2003.222.1376

• Gookin, J.L., Hanrahan, K., & Levy, M. G. (2017). The conundrum of feline trichomonosis. *Journal of Feline Medicine and Surgery*, 19(3), 261 274. https://doi.org/10.1177/1098612X17693499

• Gookin, J. L., Stauffer, S. H., Coccaro, M. R., Poore, M. F., Levy, M. G., & Papich, M. G. (2007). Efficacy of tinidazole for treatment of cats experimentally infected with *Tritrichomonas foetus*. *American Journal of Veterinary Research*, 68(10), 1085 1088. https://doi.org/10.2460/ajvr.68.10.1085

• Gookin, J.L., Stebbins, M. E., Hunt, E., Burlone, K., Fulton, M., Hochel, R., Talaat, M., Poore, M., & Levy, M. G. (2004). Prevalence of and Risk Factors for *Feline Tritrichomonas foetus and Giardia Infection*. *Journal of Clinical Microbiology*, 42(6), 2707 2710. https://doi.org/10.1128/jcm.42.6.2707-2710.2004

• Gruffydd-Jones, T., Addie, D., Belák, S., Boucraut-Baralon, C., Egberink, H., Frymus, T., Hartmann, K., Hosie, M. J., Lloret, A., Lutz, H., Marsilio, F., Möstl, K., Pennisi, M. G., Radford, A. D., Thiry, E., Truyen, U., & Horzinek, M. C. (2013). Tritrichomoniasis in cats: ABCD guidelines on prevention and management. *Journal of Feline Medicine and Surgery*, 15(7), 647 649. https://doi.org/10.1177/1098612X13489231

• Kingsbury, D. D., Marks, S. L., Cave, N. J., & Grahn, R. A. (2010). Identification of Tritrichomonas foetus and Giardia spp. Infection in pedigree show cats in New Zealand. *New Zealand Veterinary Journal*, 58(1), 6 10. https://doi.org/10.1080/00480169.2010.65054

• Kuehner, K. A., Marks, S. L., Kass, P. H., Sauter-Louis, C., Grahn, R. A., Barutzki, D., & Hartmann, K. (2011). *Tritrichomonas foetus* infection in purebred cats in Germany: Prevalence of clinical signs and the role of co-infection with other enteroparasites. *Journal of Feline Medicine and Surgery*, 13(4), 251 258. https://doi.org/10.1016/j.jfms.2010.12.002

• LeVine, D. N., Papich, M. G., Gookin, J. L., Davidson, G. S., Davis, J. L., & Hayes, R. B. (2011). Ronidazole pharmacokinetics after intravenous and oral immediate-release capsule administration in healthy cats. *Journal of Feline Medicine and Surgery*, 13(4), 244 250. https://doi.org/10.1016/j.jfms.2010.12.001

•Lionetti, E., Miniello, V. L., Castellaneta, S. P., Magistá, A. M., de Canio, A., Maurogiovanni, G., Ierardi, E., Cavallo, L., & Francavilla, R. (2006). *Lactobacillus reuteri* therapy to reduce side-effects during anti-*Helicobacter pylori* treatment in children: A randomized placebo controlled trial. *Alimentary Pharmacology & Therapeutics*, 24(10), 1461 1468. https://doi.org/10.1111/j.1365-2036.2006.03145.x

• Mammeri, M., Chevillot, A., Thomas, M., Polack, B., Julien, C., Marden, J.-P., Auclair, E., Vallée, I., & Adjou, K. T. (2018).

Efficacy of chitosan, a natural polysaccharide, against *Cryptosporidium parvum* Iin vitro and in vivo in neonatal mice. *Experimental Parasitology*, 194, 1 8. https://doi.org/10.1016/j.exppara.2018.09.003

• Pennisi, M. G., Napoli, E., Ingrà, L. a. M., & Persichetti, M. F. (2012). *Pilot Study on Efficacy and Safety of Tinidazole against Natural Tritrichomonas foetus Infection in Cats*. ISFM Congress 2012, Budapest, Hunguary. https://doi.org/10.1177/1098612X12455302

• Rosado, T. W., Specht, A., & Marks, S. L. (2007). Neurotoxicosis in 4 cats receiving ronidazole. *Journal of Veterinary Internal Medicine*, 21(2), 328 331. https://doi.org/10.1892/0891-6640(2007)21[328:nicrr]2.0.co;2

• Royal Canin. (2025). *Fecal charts cat*. https://mymvta.ca/wp-content/uploads/2021/01/Royal-Canin-GI-Fecal-Charts_Cat_English.pdf

• Sivamaruthi, B. S., Kesika, P., Chaiyasut, C., Fukngoen, P., & Sisubalan, N. (2025). A Review of Probiotic Supplementation and Its Impact on the Health and Well-Being of Domestic Cats. *Veterinary Sciences*, 12(8). https://doi.org/10.3390/vetsci12080703

• Stokes, J. E., Price, J. M., & Whittemore, J. C. (2017). Randomized, Controlled, Crossover trial of Prevention of Clindamycin Induced Gastrointestinal Signs Using a Synbiotic in Healthy Research Cats. *Journal of Veterinary Internal Medicine*, 31(5), 1406 1413. https://doi.org/10.1111/jvim.14795

• Sui, Y., Song, P., Chen, G., Zuo, S., Liu, H., Guo, J., Chang, Z., Dai, H., Liu, F., & Dong, H. (2024). Gut microbiota and *Tritrichomonas foetus* infection: A study of prevalence and risk factors based on pet cats. *Preventive Veterinary Medicine*, 226, 106162. https://doi.org/10.1016/j.prevetmed.2024.106162

• Zanzani, S. A., Gazzonis, A. L., Scarpa, P., Olivieri, E., Balzer, H.-J., & Manfredi, M. T. (2016). Coinfection with *Tritrichomonas foetus* and *Giardia duodenalis* in Two Cats with Chronic Diarrhea. *Case Reports in Veterinary Medicine*, 2016, 5705168. https://doi.org/10.1155/2016/5705168