REVIEW ARTICLE

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Gastro Retentive Drug Delivery System for Canines: A Review

Gopi Krishna Kunchala[1*], Madhuri Kosaraju[2], Gopi Ram Derangula[3]

[1*]Department of Pharmaceutical Sciences, University of Greenwich, London, United Kingdom.

[2]Department of Pharmaceutical Analysis, Narasaraopeta Institute of Pharmaceutical Sciences, Narasaraopeta, Andhra Pradesh, India.

[3] Department of Pharmaceutical Sciences, KC Reddy Institute of Pharmaceutical Sciences, Guntur, India.

ABSTRACT

The earliest ideas for gastro retentive drug delivery systems (GRDDS) were established over five decades ago. Despite substantial study in this area, still, no formulation approach has been proven to cause dependable gastro retention across various prandial settings. As a result, gastro retention is still considered the pinnacle of oral medication administration. The importance of developing medicinal products that satisfy the treatment goals of animal health, as well as attempts to enhance our knowledge of the features of using a dog as an animal model during pharmaceutical product development in human medicine, has attracted attention to the factors impacting GI transit time in canines. Several variables impact the gastrointestinal transit time in dogs and other canines. This review highlights some of these factors along with strategies to be considered during the formulation and evaluation of GRDDS for use in canines

Keywords: Canines, gastro retentive drug delivery system (GRDDS), dogs, retention, floating drug delivery system (FDDS).

1. INTRODUCTION

For over five decades, pharmaceutical experts have been working on developing approaches for extending the gastric transit length of drug formulations.[1] Gastro retention, or the longer retention of drug formulations in the gut, could have a wide range of clinical and biological effects. Enhanced local drug action in the gastrointestinal tract (GIT), lessened variations in drug levels in the blood, better patient compliance because of low dosing frequency, or enhanced rate of absorption for drugs with poor absorption in the upper GIT, and also the possibility to permit stomach-specific action, are just a few of these benefits.[2] The development of gastro retentive drug delivery systems (GRDDS) as a novel strategy for the controlled release of various medicines was pioneered.[3,4] Such systems can remain in the GIT for a prolonged time to deliver the active pharmaceutical ingredient (API) from its dosage form into the GIT.[5,6] These devices can release medications at the chosen pace and uptake region for a perpetuated length of time.[7]

1.1. Gastric Retention in Canines

The GIT of dogs is short and uncomplicated. The small intestine of a Beagle dog measures 225-290 cm in length, with the duodenum comprising 25 cm in length and the ileum being 15 cm long. Dogs have a stomach structure that is comparable with that of men. Since the sequence of the evacuation mechanism in humans and dogs in the fasting period is comparable, dogs have been formerly utilized to investigate the pharmacokinetic efficiency of new medications formulated in GRDDS. Because the dog's pylorus is shorter, gastro-retentive dosage forms (GRDFs) have a longer stomach retention period. The anatomy of Canine's GIT is shown in Figure 1.

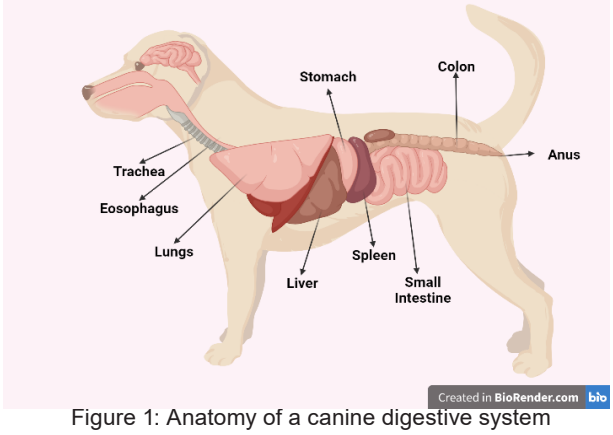

Figure 1: Anatomy of a canine digestive system

Corresponding author
Gopi Krishna Kunchala
Email: Kunchala806@gmail.com

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Despite the dog's seeming extraordinary capacity to push massive, thick objects out of the GIT, the canine stomach is often far more limited.[8] The canine pylorus varies from that of humans in its limiting character. It won't let particles flow easily through the duodenum unless their diameter is ≤ 2–3 mm.[9] As a result, several modified-release dose formulations employed in humans are simply ineffective in dogs. This is especially true for big disintegrating tablets which are meant to dissolve in the small intestinal lumen.

The absorption and effectiveness of oral medications in dogs are influenced by three key factors: canine physiological circumstances, pharmacological characteristics, and oral preparations. Changes in medication effectiveness are caused by changes in gastrointestinal pH and gastric emptying. Canine species, sex, age, and food all have an impact on their physiological state, resulting in a variety of absorptions.

Body sizes/weights largely vary among the canine population, and there is a dearth of clear information concerning the impact of body size on gastric emptying/transit periods. The association between body size and GIT transit durations is fairly little studied. Gastric emptying and transit time estimations in dogs might also differ based on the study technique. The following are some of the approaches for studying gastric emptying:[10]

- γ-scintigraphy.
- Radiographic imaging [e.g., use of barium impregnated polystyrene spheres (BIPS) or other radio-opaque materials].
- Tracer studies (13C-labeled substances).
- Administration of telemetric capsule (e.g., SmartPill, BravoTM capsule) to monitor internal pH and transit.

2. FACTORS AFFECTING GASTRIC RETENTION IN CANINES

Gastric retention in canines is dependent on various factors such as the presence or absence of food, nature, the viscosity of food, physiology, stress, and environment (Figure 2).

2.1. Particle Size

The particle size is simply among the many important factors that determine the pace of material transit in dogs. The fluidity of the gastric secretions, the density of the particles, the presence/absence of food, the amount of the gastric contents, and the geometry and suppleness of the "particle" are all relevant factors. Also, when particles are homogeneous, the timing of administration of drugs with the commencement of the housekeeping wave affects emptying.[11]

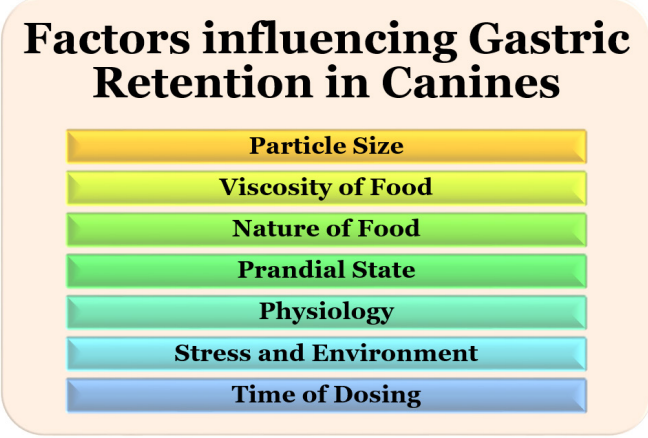

Figure 2: Factors influencing Gastric Retention in Canines

2.2. Viscosity of Food

High-viscosity foods can impact GI motility by delaying gastrointestinal transit, which is more prominent in dogs than in humans.[12] The preponderance of canine foods has a viscosity of around 100 cps and leads to a minor rise in the viscosity of the stomach contents, hence this viscosity impact is uncertain to have therapeutic significance in canines.

2.3. Nature of food

Fluids, digested food, and undigested materials are all evacuated in different stages, with the liquids exiting much faster than solid food.[13] Because liquids and solids empty independently, eating should have little effect on the pattern of the plasma concentration/time profiles of extremely soluble substances.

2.4 Fed/ Fasting state

When given to fasting dogs, soluble acetaminophen powder, enteric-coated pyridoxal phosphate tablets, and aspirin granules were quite well up took, but the meal had a significantly varied impact on the uptake of these 3 separate pharmaceutical formulations, according to Kaniwa et al.[14] Although particles less than 10 mm in size might be evacuated with the housekeeping wave in fasting dogs (about 1.5 hours), particles above 5 mm in size were held for more than 7.5 hours when given in a fed state, according to Itoh et al.[15] Gas-producing devices extended the mean gastric retention period in fasting dogs by up to 4 hours in vivo studies.[16]

2.5 Physiology

The activation of chemosensors in the upper small intestine causes nutrient-rich foods to produce a latency in gastric emptying. The biological control of gastric evacuation tends to be dominated by the nature of the

food. Ingesting lipids has been shown to impede gastric emptying, most likely due to reflexive responses induced by lipolytic chemicals released due to pancreatic lipases acting in the small intestine.[17]

2.6. Stress and environment

The pace of gastrointestinal evacuation can be slowed in experimental situations that promote the production of stress hormones.[18] Transporting dogs to an unfamiliar location can reduce antropyloral muscle movements, lengthening GI transit time.

3. GRDDS FOR CANINES

GRDDS have been developed for canines to help in the uptake of medications with limited absorption, as well as for treating upper gastrointestinal illnesses.[19] Klausner et al. found that there are two crucial aspects to consider when designing innovative unfolding GRDDS in dogs: geometrical proportions and stiffness of formulation.[20] It was determined that measures about 2.5 cm x 2.5 cm or more were necessary to be kept in the canine gut constantly. Moreover, the use of solid polymeric sheets prevented muscular contractions from pulverizing the dosage form down to smaller sizes, resulting in a longer gastric residence duration. The intriguing result is these systems can be kept in the stomachs of fed canines for over 24 hours, even though they were still reliant on the availability of food.

Drug particles have been found to linger in the gastrointestinal area for a minimum of 24 hours in smaller animals, such as dogs, enabling controlled delivery of medicines that have limited absorption to optimize therapeutic effects, such as furosemide and levodopa.[21] As opposed to twice-daily dosing, El-said developed a super porous hydrogel (SPH) mixed system, analyzed baclofen delivery, and assessed transit time in the stomach area for minimum 6hrs with enhanced protracted drug release as well as persistent plasma levels.[22] In comparison with people, swine, or bunnies, the problem with drug delivery in the canine gut is residence time, since they are reported to have quick gastric motility and less GI transit periods, as well as reasonably powerful migratory motor complexes.[23] Cargill evaluated a 24 hr residence time in beagle dogs and found that formulation design, size, and stiffness impact gastric retention times.[24]

GRDDS help to extend drug stay in the stomach, which might be necessary to get optimum therapeutic advantages of medications uptook from the upper section of the GIT.[25] During the past 30 years, floating drug delivery systems (FDDS),[26] expanding and swelling systems,[27,28] hydrogel systems,[29] and other hampered gastric evacuation techniques have all been seeking to strengthen the duration of an oral dose formulation in the gut. The different types of GRDDS are depicted in Figure 3.

Types of GRDDS	Floating Drug Delivery Systems
	Expandable Unfoldable Systems
	Magnetic Systems
	Raft Forming Systems
	Swelling Systems
	Muco-adhesive Systems
	Superporous Hydrogel Systems
	High Density Systems

Figure 3: Types of GRDDS

Floating Drug Delivery Systems (FDDS)

FDDS are oral drug delivery systems that allow for about 12 hours of stomach retention. The medicament is kept inside the empty central core of the buoyant microsphere and delivered slowly into the gut. The residual system is purged when the medication is released into the stomach. Nevertheless, many findings demonstrate that the prandial status has a significant impact on system retention and that the drug transits more quickly in starving conditions vs fed conditions. Because of their buoyant qualities that can be obtained in a variety of ways FDDS are kept in the GIT for a longer time.[30] In dogs, the relative bioavailability of furosemide using marketed products and an FDDS formulation was evaluated by Menon et al.[31] The feature that proximal GIT is the principal route of uptake for furosemide has been ascribed to greater bioavailability of FDDS forms versus marketed products.

Limitations of FDDS:

Among the drawbacks of FDDS is that they necessitate a significant amount of gastric fluids for the medication to float on and function properly. This constraint can be solved by covering the dose formulation with mucoadhesive polymers, allowing them to attach to the mucosal membrane of the stomach .[32] For medications with absorption or stability issues in stomach fluids, FDDS are not an option. Also, there are restrictions on the use of FDDS for medications that irritate the stomach mucosal lining.[33]

Extended-Release Drug delivery system (ERDDS)

Once-daily dosing is the goal of extended-release drug delivery systems (ERDDS). Despite the vast variations in digestive structure and functioning between dogs and humans, finding demonstrates that GI transit of an

Table 1: GRDDS formulations of drugs used in veterinary medicine (dogs)

Drug	*Disease*	*Controlled release system*	*Effects*	*References*
Theophylline	Asthma	Extended-release	Maintain plasma concentration of drug in therapeutic limit	37
Nizatidine	Gastric and duodenal ulcers	Floating microspheres	Controlled the drug release	38,39
Hydromorphone	Analgesia	Extended-release	Gastric retention of about 6 h	40
Mebeverine HCl	Irritable bowel syndrome	FDDS formulation	Increased floating time >12 h and higher relative bio-availability	41
Apremilast	Psoriatic arthritis	Extended-release	-	42
Primaquine	Plasmodium vivax malaria	Extended-release	Improve drug efficacy and tolerability	43
Calcifediol	Chronic kidney disease	Extended-release	Increased all measured vitamin D metabolites	44
Amoxicillin	GIT infections	Swelling GRDF	Prolonged gastric retention times for more than 48 h	45

ERDDS medication can enhance serum levels in dogs.[34] ERDDS formulation of levetiracetam has been approved for use in dogs as an antiepileptic medication.[35] In dogs, the pharmacokinetic characteristics of immediate-release (IR) and extended-release (ER) preparations of levetiracetam were investigated. The discovery was not surprising, considering that ER preparations disintegrate or liberate from their formulation at a slower pace than IR forms, which would alter the rate and degree of drug uptake.[36] The GRDDS of veterinary medicines used in canines is tabulated in Table 1.

Klausner et al. proposed a GRDDS of levodopa based on unfurling polymeric membranes.[20,46] In vitro tests revealed that the drug delivery system (DDS) unfurled in 15 minutes. It was validated in beagle dogs in vivo, with the prolonged version lasting a minimum of 2 hours. The extended plasma drug levels with enhanced bioavailability were also discovered in an in vivo pharmacokinetic investigation of GRDDS of acyclovir in beagle dogs.[47] In comparison with commercially available famotidine, one more pharmacokinetic investigation in Beagle dogs revealed an SR formulation of famotidine as well as higher absorption.[48] In addition, a γ scintigraphy investigation in Beagle dogs revealed that the modified tablets persisted in the dog gut for 7 hours, indicating that the tablets are viable for potential developments.[49] Lastly, an in vivo investigation in Beagle dogs confirmed the gastro retentive membrane's capacity to assure controlled release of the drug, particularly when fed, making the created system a potential technique for stomach-targeted DDS.[50]

FORMULATION STRATEGIES

Due to their quick gastric emptying, only a few orally administered suspended release (SR) preparations have been authorized to be used in dogs.[51] The dog's small intestine transit time is around 2 hours vs 3–4 hours in people, and the overall GI transit time in dogs is about 6–8 hours compared to 20–30 hours in humans.[52] When trying to build colon-targeted DDS that must stay somewhat intact to retain their controlled-release function, the difference between human and dog pulverizing power can be especially crucial. There has been a minimal indication of an ER profile when canines were given ER theophylline preparations designed for human use. As a result, while constructing GRDDS, especially those designed for gastric retention, the significant crushing power of the canine gut must be emphasized.

There are numerous strategies for attaining GI retention that could be wise to emphasize to solve this difficulty.[53] Particle buoyancy, settling, mucosa adherence, inflating, and swelling devices are examples of these systems. The levodopa GRDDS form, which is designed to stretch to a diameter of 5 cm - 2.5 cm, is an instance of an expandable system. This system was effectively kept in the dog's GIT for a minimum of 24 hours, allowing the medicine, levodopa, to be released more slowly.

Particle density adjustment could be used to create FDDS that have a lengthy gastric stay. Nevertheless, the influence of the prandial condition on the functioning of such systems must be taken into account.[54] Fasting, on the other hand, had a considerable effect on the effectiveness of SPH in gelatin capsules.[55] The SPH expands to a diameter that promotes residence time when exposed to gastric juices. The SPH system stayed in the stomach for over 2–3 hours after being given to dogs, following which it was pulverized and broken up into tiny pieces before being discharged into the intestinal tract. Although the fed state was only retained for a few hours, the SPH

compound persisted in the stomach for over 24hrs when meal was provided just before dosing.

An ad hoc team of the United States Pharmacopeia (USP) was recently established to clarify the requirements for medicines with greater solubility and permeability in dogs. This canine-adjusted biopharmaceutical classification system (BCS) would be extremely useful in forecasting medicine bioavailability in animals, as well as in cases where stomach retention time seems to be the rate-limiting stage in drug uptake. The findings will influence the productivity of sustained-release orally administered formulations by revealing the various elements that influence canine stomach transit time. Finally, adjusting the BCS for canine metabolism is expected to aid in the prediction of drug biological activity and scenarios wherein canine drug uptake vary from those of humans.

5. IN VITRO AND IN VIVO EVALUATION

For extrapolating in vivo activity, in vitro assessment must preferably imitate physiological settings as nearly as feasible. Since the generally utilized equipment described by the USP is unfit for imitating some aspects such as GIT motility or "peristaltic force" of the gut, whether in vitro findings correlate to in vivo studies is questionable.[56] Any dosage form must undergo in vitro release analysis to have a better knowledge of the drug in vivo delivery. In vitro investigations are used to determine how well a medication is delivered from its formulation.[57] Nevertheless, in vitro assays that more precisely resemble GIT metabolism than the traditional USP system have been established. Because of their well-specified GI physiology and ability to swallow medicines, the beagle dog is commonly employed for in vivo research. Further advantages of the beagle dog include the aspect that it is a tiny to medium-sized species with a kind disposition, making it simple to handle and house.

The ability to establish bioequivalence among breeds by an inexpensive and convenient method of in vitro and in vivo correlation (IVIVC) is a critical requirement in the preparation of drugs for dogs.[58] While there are multiple occurrences of human IVIVC, data for the dog model is scarce. Jinno et al.[59] discovered a connection between cilostazol size reduction with in vitro dissolution and in vivo efficacy in beagle dogs in their study. The analysis revealed that increasing the pace at which a medicine dissolves can lessen the impact of meals on the solubility of a poorly soluble agent. This may result in a higher IVIVC in fed canines. Nevertheless, this research concluded no significant link between in vitro and in vivo disintegration, which is a challenge associated with all IVIVC investigations.

Ghimire et al.[60] explored how well a double-compressed pulsatile release theophylline tablet has performed in vitro. Using pharmacoscintigraphy, the researchers have been able to acquire parallel findings in beagle dogs. In comparison to the in-vitro lag time (72 ± 8 min), they discovered no substantial change in the in-vivo lag periods of both fasting (89 ± 13 min) and fed stages (79 ± 11 min). The research demonstrates that a very excellent IVIVC may be achieved if drug release characteristics are irrespective of pH, crushing force, and fat content.

McInnes *et al.*[61] demonstrated that in vitro findings do not always necessarily correspond to in vivo results. During the first 2 hours, the in vitro release of the first formulation (F-1) was similar to that of in vivo, but after that, the in vitro drug release was quicker than that of in vivo. In both fasting and fed canines, the in vitro drug release from the second formulation (F-2) was much steadier than the in vivo drug release; furthermore, the release was even faster in fed dogs. In vivo, F-2 released substantially faster than F-1, but F-1's in vitro release was much greater. It was an unexpected discovery. The in vivo activities of these formulations were uncovered during the scintigraphic examination, which confirmed these interesting findings.

Takano's team looked at the rate-determining steps of three BCS class II medicines both in vivo and in vitro.[62] The findings of in vitro modeled evaluation were found to match up with in vivo results in the research. This motivates scientists to investigate and improve in vitro modeling settings for in vivo matching. Setting up a proper in vitro assessment system is difficult. Nevertheless, full knowledge of the elements that determine the API's in vitro dissolution pattern allows for a precise estimate of in vivo activity.

6. CONCLUSION

The international market for dog care has been predicted to increase dramatically in the foreseeable future as dog owners' needs and expectations rise. Pharmaceutical experts are embracing ever more revolutionary pharmaceutical innovations to promote medical performance and enhance dog and owner conformity to produce an optimal veterinary therapy, which is challenging the principles of standard drug formulations and their marketing. By improving medication stay in the stomach, a GRDDS device has the potential to provide increased bioavailability and regulated drug administration. With the advancement of delivery systems, a greater variety of GRDDS would be developed to optimize the administration of compounds with a narrow absorption, limited solubility, and heavy first-pass effect.

REFERENCES:

1. Schneider F, Koziolek M, Weitschies W. In vitro and in vivo test methods for the evaluation of gastroretentive dosage forms. Pharmaceutics. 2019;11(8):416.
2. Bermejo M, Sanchez-Dengra B, Gonzalez-Alvarez M, Gonzalez-Alvarez I. Oral controlled release dosage forms: dissolution versus diffusion. Expert Opinion on Drug Delivery. 2020;17(6):791-803.
3. Vrettos NN, Roberts CJ, Zhu Z. Gastroretentive technologies in tandem with controlled-release strategies: A potent answer to oral drug bioavailability and patient compliance implications. Pharmaceutics. 2021;(10):1591.
4. Ibrahim M, Naguib YW, Sarhan HA, Abdelkader H. Gastroretentive oral drug delivery systems: a promising approach for narrow absorption window drugs. Journal of Advanced Biomedical and Pharmaceutical Sciences. 2019 Jul 1;2(3):98-110.
5. Kumar M, Kaushik D. An overview on various approaches and recent patents on gastroretentive drug delivery systems. Recent patents on drug delivery & formulation. 2018;12(2):84-92.
6. Gadge G, Sabale V, Khade A, Mahajan U. Current Approaches on Gastro Retentive Drug Delivery System: An Overview. International Journal of Pharmacy Research & Technology. 2019;9(2):16-28.
7. Tripathi J, Thapa P, Maharjan R, Jeong SH. Current state and future perspectives on gastroretentive drug delivery systems. Pharmaceutics. 2019;(4):193.
8. Morelli S, Diakou A, Di Cesare A, Colombo M, Traversa D. Canine and feline parasitology: Analogies, differences, and relevance for human health. Clinical microbiology reviews. 2021;34(4):e00266-20.
9. Hoskins JD. The digestive system. Veterinary pediatrics. 2001:147.
10. Wyse CA, McLellan J, Dickie AM, Sutton DG, Preston T, Yam PS. A review of methods for assessment of the rate of gastric emptying in the dog and cat: 1898–2002. J Vet Int Med. 2003;17:609–621.
11. Martinez MN, Papich MG. Factors influencing the gastric residence of dosage forms in dogs. Journal of pharmaceutical sciences. 2009;98(3):844-60.
12. Dressman JB. Comparison of canine and human gastrointestinal physiology. Pharmaceutical Research. 1986;3(3):123-31.
13. Abrahamsson B, Albery T, Eriksson A, Gustafsson I, Sjo¨berg M. 2004. Food effects on tablet disintegration. Eur J Pharm Sci. 2004;22:165–172
14. Kaniwa N, Aoyagi N, Ogata H, Ejima A. 1988. Gastric emptying rates of drug preparations. I. Effects of size of dosage forms, food and species on gastric emptying rates. J Pharmacobiodyn. 1988;11:563–570.
15. Itoh T, Higuchi T, Gardner CR, Cladwell L. 1986. Effect of particle size and food on gastric residence time of non-disintegrating solids in beagle dogs. J Pharm Pharmacol. 1986;38:801–806.
16. Baumgartner S, Kristl J, Vrecer F, Vodopivec P, Zorko B. Optimisation of floating matrix tablets and evaluation of their gastric residence time, Int. J. Pharm. 2000;195(1 – 2):125 – 135.
17. Van Citters GW, Lin HC. Ileal brake: neuropeptidergic control of intestinal transit. Current gastroenterology reports. 2006;8(5):367-73.
18. Gue M, Peeters T, Depoortere I, Vantrappen G, Bueno L. 1989. Stress-induced changes in gastric emptying, postprandial motility, and plasma gut hormone levels in dogs. Gastroenterology. 1989;97:1101–1107.
19. Garg RG, Gupta GD. Progress in controlled gastroretentive delivery systems. Tropical journal of pharmaceutical research. 2008;7(3):1055-66.
20. Klausner, E. A., Eyal, S., Lavy, E., Friedman, M. & Hoffman, A. Novel levodopa gastroretentive dosage form: in-vivo evaluation in dogs. J. Control. Release. 2003;88:117–126.
21. Hayward A, Bensel T, Mazdiyasni H, Rogner J, Kirtane AR, Lee YA, Hua T, Bajpayee A, Collins J, McDonnell S, Cleveland C. Scalable gastric resident systems for veterinary application. Scientific reports. 2018;8(1):1-0.
22. El-Said, I. A., Aboelwafa, A. A., Khalil, R. M. & ElGazayerly, O. N. Baclofen novel gastroretentive extended release gellan gum superporous hydrogel hybrid system: in vitro and in vivo evaluation. Drug Deliv. 2016;23:101–112.
23. Aoyagi, N. et al. Gastric emptying of tablets and granules in humans, dogs, pigs, and stomach-emptying-controlled rabbits. J. Pharm. Sci. 1992;81:1170–1174.
24. Cargill, R. et al. Controlled Gastric Emptying. 1. Effects of physical properties on gastric residence times of nondisintegrating geometric shapes in beagle dogs. Pharm. Res. 1988;5:533–536.
25. Zanke AA, Gangurde HH, Ghonge AB, Chavan PS. Recent Advance in Gastroretantive Drug Delivery System (GRDDS). Asian Journal of Pharmaceutical Research. 2022;12(2):143-9.
26. Bhosale AR, Shinde JV, Chavan RS. A Comprehensive Review on Floating Drug Delivery System (FDDS). Journal of Drug Delivery and Therapeutics. 2020;10(6):174-82.
27. Mehta M, Pandey P, Mahajan S, Satija S. Gastro retentive drug delivery systems: An overview. Research Journal of Pharmacy and Technology. 2018;11(5):2157-60.
28. Gopalakrishnan S, Chenthilnathan A. Floating drug delivery systems: A Review. Journal of Pharmaceutical science and technology. 2011;3(2):548-54.
29. Mayur C, Senthilkumaran K, Hemant G. Super porous hydrogels: a recent advancement in gastroretentive drug delivery system. Indonesian Journal of Pharmacy. 2013;24(1):1-3.
30. Singh BN, Kim KH. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. Journal of Controlled release. 2000;63(3):235-59.
31. Menon, A.; Wolfgang, A.; Ritschel, A.; Sakr, A. Development of and evaluation of a monolithic floating dosage form for furosemide. J. Pharm. Sci. 1994;83:239– 245.
32. Sarjavalagi VG, Chaurasia PK, Harshitha AP, Singh SS, Sonar NS. A Systematic Review. Asian Journal of Pharmacy and Technology. 2020;10(4).
33. Pawar VK, Kansal S, Garg G, Awasthi R, Singodia D, Kulkarni GT. Gastroretentive dosage forms: A review with special emphasis on floating drug delivery systems. Drug delivery. 2011;18(2):97-110.
34. Beasley MJ, Boothe DM. Disposition of extended release levetiracetam in normal healthy dogs after single oral dosing. Journal of Veterinary Internal Medicine. 2015;29(5):1348-53.
35. Muñana KR, Otamendi AJ, Nettifee JA, Papich MG. Population pharmacokinetics of extended-release levetiracetam in epileptic dogs when administered alone, with phenobarbital

or zonisamide. J Vet Intern Med. 2018;32(5):1677-1683. doi: 10.1111/jvim.15298.

36. Boozer LB, Platt SR, Haley AC, et al. Pharmacokinetic evaluation of immediate- and extended-release formulations of levetiracetam in dogs. Am J Vet Res. 2015;76(8):719-723. doi:10.2460/ajvr.76.8.719
37. Bach JF, Kukanich B, Papich MG, McKiernan BC. Evaluation of the bioavailability and pharmacokinetics of two extended-release theophylline formulations in dogs. Journal of the American Veterinary Medical Association. 2004;224(7):1113-9.
38. Rajpali, D. and Gupta, V., 2020. Floating Microspheres Based Nizatidine Gastro Retentive Formulation to Control the Release of Drug. Letters in Applied NanoBioScience. 9. 1409-1419. 10.33263/LIANBS93.14091419.
39. Balata, Gehan. Design and evaluation of gastroretentive floating tablet of nizatidine: A trial to improve its efficacy. International Journal of Pharmacy and Pharmaceutical Sciences. 2014;6:423-429.
40. Wunsch LA, Schmidt BK, Krugner-Higby LA, Smith LJ. A comparison of the effects of hydromorphone HCl and a novel extended release hydromorphone on arterial blood gas values in conscious healthy dogs. Res Vet Sci. 2010;88(1):154-158. doi:10.1016/j.rvsc.2009.07.008
41. El Nabarawi MA, Teaima MH, Abd El-Monem RA, El Nabarawy NA, Gaber DA. Formulation, release characteristics, and bioavailability study of gastroretentive floating matrix tablet and floating raft system of Mebeverine HCl. Drug Des Devel Ther. 2017;11:1081-1093. doi:10.2147/DDDT.S131936
42. Tang M, Hu P, Huang S, Zheng Q, Yu H, He Y. Development of an Extended-Release Formulation for Apremilast and a Level A in Vitro-in Vivo Correlation Study in Beagle Dogs. Chem Pharm Bull (Tokyo). 2016;64(11):1607-1615. doi:10.1248/cpb.c16-00519
43. Bertol CD, Oliveira PR, Kuminek G, Rauber GS, Stulzer HK, Silva MA. Increased bioavailability of primaquine using poly(ethylene oxide) matrix extended-release tablets administered to beagle dogs. Ann Trop Med Parasitol. 2011;105(7):475-484. doi:10.1179/2047773211Y.0000000003
44. Parker VJ, Rudinsky AJ, Benedict JA, Beizaei A, Chew DJ. Effects of calcifediol supplementation on markers of chronic kidney disease-mineral and bone disorder in dogs with chronic kidney disease. J Vet Intern Med. 2020;34(6):2497-2506. doi:10.1111/jvim.15949
45. Horwitz E, Kagan L, Chamisha Y, Gati I, Hoffman A, Friedman M, Lavy E. Novel gastroretentive controlled-release drug delivery system for amoxicillin therapy in veterinary medicine. Journal of Veterinary Pharmacology and Therapeutics. 2011;34(5):487-93.
46. Klausner EA, Lavy E, Barta M, Cserepes E, Friedman M, Hoffman A. Novel gastroretentive dosage forms: evaluation of gastroretentivity and its effect on levodopa absorption in humans. Pharm. Res. 2003;20 (9):466 – 1473.
47. Shin S, Kim TH, Jeong SW, et al. Development of a gastroretentive delivery system for acyclovir by 3D printing technology and its in vivo pharmacokinetic evaluation in Beagle dogs. PLoS One. 2019;14(5):e0216875. Published 2019 May 15. doi:10.1371/journal.pone.0216875
48. Guan, J.; Zhou, L.; Pan, Y.; Han, H.; Xu, H.; Pan, W. A Novel Gastro-Retentive Osmotic Pump Capsule Using Asymmetric Membrane Technology: In Vitro and In Vivo Evaluation. Pharm. Res. 2009;27:105.
49. Guan, J.; Zhou, L.; Nie, S.; Yan, T.; Tang, X.; Pan, W. A novel gastric-resident osmotic pump tablet: In vitro and in vivo evaluation. Int. J. Pharm. 2010;383: 30–36.
50. Hwang KM, Nguyen TT, Seok SH, Jo HI, Cho CH, Hwang KM, Kim JY, Park CW, Rhee YS, Park ES. Swellable and porous bilayer tablet for gastroretentive drug delivery: Preparation and in vitro-in vivo evaluation. International Journal of Pharmaceutics. 2019;572:118783.
51. Shanmugam S, Ryu JK, Yoo SD, Choi HG, Woo JS. Evaluation of pharmacokinetics of simvastatin and its pharmacologically active metabolite from controlled-release tablets of simvastatin in rodent and canine animal models. Biomolecules & Therapeutics. 2011;19(2):248-54.
52. Bagul US, Patil RV, Shirsath YA, Nikam AJ, Gujar KN. Stomach specific drug delivery systems: a review. Int J Pharm Res Dev. 2011;4(4):147-50.
53. Davis SS. Formulation strategies for absorption windows. Drug discovery today. 2005;10(4):249-57.
54. Vivek R. Effect of Food through Drug Delivery System. J Bioequiv Availab. 2021;13:426.
55. Chen J, Blevins WE, Park H, Park K. Gastric retention properties of superporous hydrogel composites. *Journal of controlled release*. 2000;64(1-3):39-51.
56. Song Y, Peressin K, Wong PY, Page SW, Garg S. Key considerations in designing oral drug delivery systems for dogs. Journal of Pharmaceutical Sciences. 2016;105(5):1576-85.
57. Higgins GS, Rathbone MJ, Brumfield JC. In vitro drug release testing of veterinary pharmaceuticals. In: Rathbone MJ, McDowell A, eds. Long Acting Animal Health Drug Products. Boston, MA: Springer; 2013:193-220
58. Emami J. In vitro - in vivo correlation: from theory to applications. J Pharm Pharm Sci. 2006;9(2):169-189.
59. Jinno J, Kamada N, Miyake M, et al. Effect of particle size reduction on dissolution and oral absorption of a poorly water-soluble drug, cilostazol, in beagle dogs. J Control Release. 2006;111(1-2):56-64.
60. Ghimire M, McInnes FJ, Watson DG, Mullen AB, Stevens HN. In-vitro/in-vivo correlation of pulsatile drug release from press-coated tablet formulations: a pharmacoscintigraphic study in the beagle dog. Eur J Pharm Biopharm. 2007;67(2):515-523.
61. McInnes F, Clear N, Humphrey M, Stevens HN. In vivo performance of an oral MR matrix tablet formulation in the beagle dog in the fed and fasted state: assessment of mechanical weakness. Pharm Res. 2008;25(5): 1075-1084.
62. Takano R, Furumoto K, Shiraki K, et al. Rate-limiting steps of oral absorption for poorly water-soluble drugs in dogs; prediction from a miniscale dissolution test and a physiologically-based computer simulation. Pharm Res. 2008;25(10): 2334-2344.

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