Indonesian Journal of Pharmaceutics
IdJP
ISSN : 2597-8748

Vol 4, Issue 4, 2023 (333-346)
http://journal.unpad.ac.id/idjp

Drug Delivery System in Feline

Yedi Herdiana[1,2*], Gofarana Wilar[2,3], Ferry Ferdiansyah Sofian[4], Annisa Dyah Pitaloka[4], Yasinta Nurhijriah[4], Rayhan Zarra Safira[4], Annisa Siti Salsabila[4], Maziyatunisa Z[4]

[1] Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang 45363, Indonesia.
[2] Veterinary Center Development Group, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang 45363, Indonesia.
[3] Department of Pharmacology and clinical pharmacy, Fakulty of Pharmacy, Universitas Padjadjaran Sumedang 45363, Indonesia.
[4] Faculty of Pharmacy, Universitas Padjadjaran

Submitted : 05/01/2023, Revised : 03/02/ 2023,, Accepted : 14/03/2023, Published : 16/08/2023

Abstract

The drug delivery system is an attractive field of study since it has several applications in veterinary and human medicine. In the realm of veterinary medicine, the discovery of new routes of administration or new delivery systems to regulate the release of medications is of great importance. Due to the high number of animals and the special issues related to the administration of drugs and their market potential is very large, it is necessary to modify the dosage form to produce an effective and practicable preparation. Cats are the most popular pet in the world, outnumbering dogs by a ratio of three to one. It is vital to understand the prevalent illness patterns and limits of traditional delivery systems to establish appropriate dosage forms for cats. We believe this publication will be of interest to veterinarians and pharmaceutical scientists working in the field.

Keywords: Drug delivery system, cats, veterinary medicine, pharmacist

1. Introduction

In veterinary medicine, most drug formulations are of the conventional variety where some of the problems is failure to deliver and deposit the drug molecule at the desired place [1,2]. Due to the diversity of animal species, body systems, and requirements, veterinary equipment's nature and physical structure can be shaped in several ways. Improvement of animal welfare (the reduction of stress from restraints and handling required for more frequent dosing of conventional formulations), caregiver or veterinarian convenience, and a reduction in the cost of care are all potential benefits of developing a controlled and/or prolonged-release system for the veterinary field [3]. In addition, these dosage forms help decrease human exposure to potentially hazardous substances used in veterinary medicine. Nevertheless, numerous obstacles persist in the veterinary field, including restricted resources, highly competitive product pricing, getting registration, especially regarding human food safety and environmental safety, and occasionally a

*Corresponding author,
e-mail : y.herdiana@unpad.ac.id (Y. Herdiana)

https://doi.org/10.24198/idjp.v4i3.44274
© 2023 Y. Herdiana et al

mismatch between projected and actual market needs [4].

Domestic cats are popular companion animals with various lifestyles [5,6] . Felidae includes cats, is animal with 50-60 cm long, 25-28 cm tall, weighs 3-6 kg (male) and 2-4.5 kg (female), and lives 10-20 years. Purebred cats include the Persian Angora, Siamese, Manx, and Sphinx, are bred as pets. Only 1% of cats worldwide are purebred; the rest are wild or domestic cats with mixed breeds. Cats have considerable economic worth, especially for breeders and cat lovers. Cats may also improve human mental health. Caring for a cat means giving it enough food, water, and balanced nutrition. Uncared-for cats can contract diseases and spread them to humans. Cats can get sick and delaying medical attention can be deadly. It's important for cat owners to seek prompt veterinary care to ensure their pet receives the best possible treatment and lives a healthy life. Most cat owners address health problems and diseases themselves due to a lack of professionals and difficulty connecting directly with them. A lack of knowledge about cat diseases makes it difficult for owners to handle and medicate sick cats, which can exacerbate the illness. Cat diseases are caused by parasites, protozoa, germs, and other factors [7,8].

In human and veterinary medicine, most medications and formulations are given as elixirs, infusions, capsules, and aqueous or oil-based injections [6]. Because of the harmful consequences of potent or dangerous ingredients, medications must be administered with caution. Veterinary medicine administration systems differ from human medication distribution systems. The nature and shape of veterinary equipment are adaptable due to the wide range of animal species, body systems, and needs.

Pharmacists must provide scientific explanation when selling pharmaceuticals, and veterinarians have a similar responsibility to ensure the integrity of any medical product they deliver to patients. Failing to do so can pose a risk to the health and safety of patients, pet owners, and veterinarians. [9]. Novel formulation improvements, including carrier technologies, continuous-release devices, and site-directed formulations, could be employed to direct or extend animal bioavailability. Suitable technologies are required for fast, safe, efficient, and cost-effective drug delivery. This review analize illness patterns, conventional drug delivery, and novel dosage form design for veterinary application.

2. Common pattern of disease in Canine

These environmental factors and direct contact with pathogens can weaken a cat's immune system and make them more susceptible to a variety of illnesses. [10,11]. Diseases that affect cats are typically infectious or contagious. The following are some common diseases in cats.

2.1 Feline paleukopenia

Feline panleukopenia is a disease caused by the Feline Panleukopenia Virus (FPV), a member of the Parvoviridae family. Clinical symptoms vary from subclinical infection to acute, characterized by sudden death. Feline panleukopenia disease refers to low white blood cells in a cat's body. Infected cats die from complications from secondary bacterial infection, sepsis, dehydration, and disseminated intravasal coagulopathy (DIC). The level of morbidity and mortality due to feline panleukopenia is quite high, especially in young cats under 12 weeks of age. Acute feline panleukopenia has a mortality rate of 25-90% to 100% in acute infections [12,13].

2.2 Feline Calicivirus (FCV)

Feline calicivirus is a highly contagious pathogen. FCV infection can cause several clinical problems in

asymptomatic carriers. Oral ulcers, especially on the tongue and palate, and mild upper respiratory symptoms are typical. This disease is highly contagious, often fatal and results in high mortality [14,15]. This disease can attack young and adult cats, even though they have been vaccinated. FCV infection can cause severe pneumonia in kittens and rarely in adults. FCV-infected cats develop edema and ulcers on the head, limbs, soles of the feet, and inguinal area. FCV infection may produce subcutaneous edema with localized fat necrosis, pancreatitis with peripancreatic fat necrosis, DIC, intestinal crypt necrosis, and interstitial pneumonia [15,16].

2.3 Feline Infectious Peritonitis (FIP)

Feline Infectious Peritonitis (FIP) is a viral infection in cats with clinical signs of ascites occurring in an effusive form. Ascites are a common systemic condition characterized by abdominal distention due to fluid accumulation. These clinical signs are reported to be associated with chronic liver disease, congestive heart failure, nephritic syndrome, malnutrition, ancylostomiasis, low blood protein levels, especially albumin, various types of neoplasms, as well as increased renal sodium-sodium ion retention, FIP has high morbidity and mortality rate. In cats and is fatal in cats who are infected or have certain clinical signs and symptoms. More cases were reported in male and young cats under 3 years old [1,17].

2.4 Scabies (scabies)

Scabies is a cat skin disease caused by scabies/Sarcoptes mites (a type of flea). Dogs and cats are both susceptible to scabies. The parasite species that most often targets dogs (Sarcoptes scabei canis) is different from the species that tend to target cats (Notoedres cati). However, both species come from the same family of Sarcoptic mites. Scabies in cats is usually caused by Notoedres cati, which is a very small mite (0.2 – 0.4 mm) and can only be seen with a microscope or magnifying glass [18,19]

Scabies mites are transferred between cats via physical touch, and all cats exposed to Notoedres mites develop symptoms. Mite-infested cats commonly develop scabies a few weeks to a month later. Mites burrow between hair follicles, causing itching and other skin disorders. Mites lay 3-4 eggs daily in their burrows. After 4-5 days, the eggs hatch and the larvae build a hole. Mites will molt, grow, dig additional skin tunnels, and mature in 15 days [20,21].

2.5 Dermatophytosis (Ringworm)

Dermatophytosis is a skin disease caused by a fungus that can cause hair loss in cats. Dermatophytosis is excessive keratinization found on the skin's outermost surface (epidermis), including nails and hair. Dermatophytosis can be caused by infection with fungi/fungi that belong to the dermatophyte genus, including Microsporum, Trichophyton, and Epidermophyton [22]. The incidence of dermatophytosis by M. canis in cats was reported to be higher than in dogs. The study also reported that 82% of 89 positive cat samples had dermatophytosis due to M. canis. Clinical symptoms in animals with dermatophytosis are alopecia, erythema, papules, pustules, and scaly and crusty. Inflammation at the edges of the lesions found on the face and trunk is a classic type of lesion often found [23,24].

2.6 Ankylostomiasis

Ankylostomiasis is a disease caused by infection with the worm Ancylostoma spp., a parasite that most often attacks pets such as cats. Clinical symptoms in cats infected with ankylostomyosis are diarrhoea, sometimes accompanied by blood. At 10-25 days after infection, cats start to lose blood which can cause cats to suffer from anaemia, hypoproteinemia,

intestinal malabsorption and decreased immunity [25,26].

2.7 Toxocariasis

Toxocariasis is a disease caused by worms from the genus Toxocara, namely T. vitulorum, which attacks cattle. T. canis, which attacks dogs, and T. cati, which attacks cats. Infected cats eat and drink L2 embryonated eggs. Infected mothers' worm larvae move to their mammary glands, infecting kittens via milk. Paratenic hosts may also infect cats with T. cati. [27,28].

2.8 Diabetes Mellitus

Cats may also get metabolic illnesses like diabetes mellitus. DM affects the pancreas, which generates insulin and glucagon. DM is a chronic condition caused by the pancreas' failure to generate enough insulin, causing hyperglycemia and glucose intolerance. Obesity, lack of activity, and aging are major DM triggers. Older cats (10-13 years), castrated male cats, obesity, and lack of activity increase DM risk. Genetic factors also raise DM risk; Burmese cats are five times more at risk than other cats [29–31].

2.9 Cancer

Cancer is a common and major killer of household animals. Conservative estimates predict that one in ten dogs and cats will acquire a tumour. Veterinary cancer registers have been brief and erratic since 1940. [32]. Cats die from cancer. Understanding human oncogenes are critical for diagnostics, prognostics, and targeted therapies. [33].

Intestinal adenocarcinoma is the second most common cat cancer after lymphoma. 70% of colon cancers were studied. 55–76% of tumours metastasize locally and distantly. The main treatment is surgery with or without chemotherapy. Past retrospective research on prognostic variables and survival durations includes very small cat populations. However, results are widely varied, and extended life spans are typically recorded in systemic illness. Intestinal adenocarcinoma is the second most common cat cancer after lymphoma. 70% of colon cancers were studied. 55–76% of tumours metastasize locally and distantly. The main treatment is surgery with or without chemotherapy. Existing retrospective research on prognostic variables and life durations include small cat populations, but results are widely heterogeneous, and extended survival spans are typically reported in the setting of systemic illness [34].

3. Drug Dosage Form Design Consideration

Treating feline patients can be challenging due to differences in medication metabolism compared to other animals, resulting in a lack of adequate safety and dosage optimization trials for cats. Additionally, there are comparatively few licensed medications for cats, requiring reformulation of medications intended for larger animals, and delivery of medication to many cats can be difficult.

3.1 Drug metabolism in cats

Cats have a unique drug metabolism that is different from both humans and dogs, making it challenging to determine appropriate dosages for feline patients. In some cases, cat dosages are extrapolated from those used in other species. However, cats have poor glucuronidation of some xenobiotics due to a nonfunctional UGT1A6 pseudogene, which can result in insufficient drug metabolism for certain medications. This information is important for veterinarians to consider when prescribing medications for cats, as improper dosing can have negative consequences for feline health.

Table 1. Glucuronidation Capacity of Xenobiotics in Cats

Compounds	**UGT Enzyme Responsible for Humans**	**Glucuronidation in Cats**	**Due to Clinical and Dosage in Cats**
Acetaminophen	UGT1A6 (cat pseudogen)	Hepatic activity is ten times lower in cats than in dogs and humans	Three to four times less acetaminophen is poisonous to cats (60 mg/kg) than to dogs (200 mg/kg).
Morphine	UGT2B7 in humans	No glucuronide metabolites in dogs in vivo Not evaluated in cats	Like dogs, the elimination half-life of morphine in cats is 1-1.5 hours (1.2 hours).
Chloramphenicol	UGT2B7	Not directly evaluated in cats	Cats have a somewhat longer elimination half-life (4-8 hours) than dogs (1.1-5 hours)
Aspirin	Some isoforms (UGT1A6) have high affinity)	Not directly evaluated in cats	Cats have a long elimination half-life (22 hours) than dogs (5-6 hours) Four times less often in cats than in canines

3.2 Age-related treatment in cats

The neonatal period in cats and dogs is four weeks postpartum, while the pediatric period is 12 weeks. However, pharmacological research in neonate cats is scarce, which makes suggestions challenging. There are physiological variations between neonates and adults in humans, dogs, rats, and cats that need to be considered when prescribing medication to young animals.

Newborn kittens' oral absorption may differ from adult cats'. Immature gastric parietal cells in neonates, such as pups up to 5 weeks old, cause a high stomach pH. High stomach pH reduces the bioavailability of acid-dependent medications, including ketoconazole, itraconazole, and iron supplements. Therefore, medications that require an acidic environment for proper absorption may not be as effective in neonatal kittens.

Neonatal hepatic cytochrome P450 activity is lower than in 7-week-old dogs. This may delay neonatal medication clearance. Newborn kittens may have extended half-lives for medications such as lidocaine and theophylline. However, by the time most cats receive their first immunization, their livers have developed and become better equipped to metabolize medications.

Kittens have a low glomerular filtration rate (GFR) until they are 9 weeks old. Before this age, kittens may be at risk of fluid overload due to poor solute and water excretion, which can increase the risk of medication toxicity, such as aminoglycosides. Therefore, aminoglycosides should be avoided in kittens.

The elderly, both cats and humans, are at higher risk of adverse medication responses than younger adults. Dosing mistakes and

pharmacokinetic/pharmacodynamic variables contribute to some of these concerns. Geriatric cats have achieved 75% of their anticipated lifespan, and changes in renal function, hepatic blood flow, body composition, and physiological reactions occur in elderly cats and humans. Age-related renal insufficiency affects geriatric medication dosing the most. Renal insufficiency in elderly cats is likely to be considerable and may impede medication elimination, leading to increased toxicity. Enrofloxacin, given at 5 mg/kg daily, may cause retinal toxicity in older cats, and the dose-dependent ocular toxicity may be related to impaired renal clearance in elderly cats..

3.3 Behavioral problem

Small animal veterinarians are often the first point of contact for owners seeking help with behavioural issues in their pets. However, the evaluation and management of behavioural disorders may differ between general veterinary practices and specialized behavioural referral centers. For instance, separation anxiety in dogs and some types of urine marking in cats may be attributed to anxiety or stress.

Epidemiological studies conducted from the perspective of veterinary practitioners can help to identify and prioritize the most common behavioural concerns among pet owners. This information can be used to develop effective preventative and educational programs that aim to reduce pet abandonment and euthanasia. It is important to note that behavioural issues in pets can have complex underlying causes, and a thorough assessment by a veterinarian or animal behaviourist may be necessary to achieve a successful outcome. [35].

3.4 Conventional Dosage Form

Pharmaceutical dosage forms comprise active and inactive ingredients (Fig.1). Product quality and performance depend on the API, excipients, and manufacturing method. API is blended with binders, fillers, flavours, bulking agents, preservatives, and antioxidants. Before being formulated, these materials may be dried, processed, mixed, compressed, and granulated.

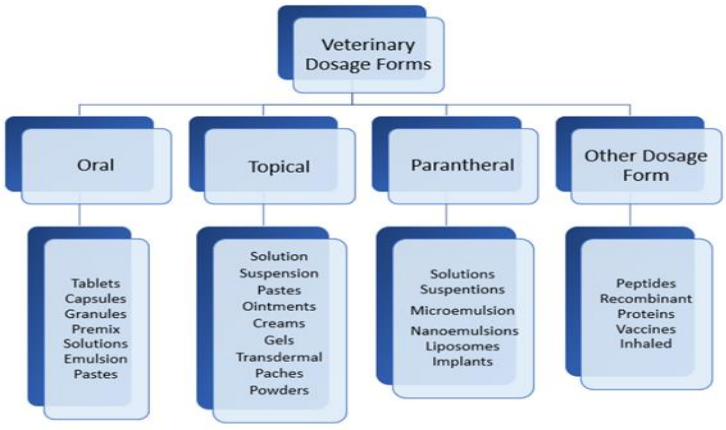

Fig 1. Common veterinary dosage forms as a function of route of administration

Drug delivery via the oral route is the most common and natural way of administering medication to pets such as dogs and cats. However, it can be challenging to ensure that pets consume their medication, which can lead to ineffective treatment. Therefore, several strategies are employed to increase compliance, including the use of flavoured

tablets or liquid formulations that are more palatable to pets.

In contrast, drug delivery systems via the parenteral route have higher bioavailability than the oral route and are essential for administering peptides and proteins. However, the parenteral route requires veterinary expertise and can lead to local irritation or inflammation at the injection site.

Topical drug delivery systems such as creams, ointments, and powders are ideal for local effects or killing parasites on the skin. These preparations are less invasive and can be used to administer local anaesthetics, but their efficacy may depend on factors such as skin type and hair density.

Transdermal drug delivery has gained popularity in veterinary medicine due to its advantages over oral and parenteral routes. Transdermal administration is often well-tolerated, has a lower risk of gastrointestinal irritation and drug degradation in the liver and gut, and may have a more extended duration of action without side effects. However, transdermal drug delivery may not be appropriate for all medications, as some may irritate the skin or have poor absorption.

Transmucosal drug administration is another method that has gained attention in recent years. This method involves the administration of medication via mucosal membranes, such as those in the mouth, nose, or rectum. This route offers the advantage of avoiding first-pass effects, liver metabolism, and stomach discomfort. However, the potential for irritation limits the use of transmucosal drug delivery for some medications.

The choice of drug delivery system depends on several factors, including the type of medication, the pet's condition, and the owner's willingness to administer the drug. It is essential to consider the risks and benefits of each method and to work closely with a veterinarian to ensure optimal treatment outcomes for pets.

4. New Drug Delivery System

The anatomical and physiological variations among different animal species can result in drug concentrations that fall outside the therapeutic range, which can ultimately cause treatment failure. To address this issue, novel drug delivery systems are being developed in veterinary medicine to adjust the drug's bioavailability for each animal, decrease the number of doses needed, minimize stress for owners, and reduce the overall duration of treatment. [36]. In addition, the development of drug delivery systems specific to different animals and their unique physiological characteristics can improve the effectiveness and safety of drug administration. For example, transdermal drug delivery may be a suitable alternative for cats who are difficult to medicate orally or intravenously, but it may not be appropriate for other animals due to differences in skin thickness and permeability. By considering the anatomical and physiological differences between animals and developing tailored drug delivery systems, veterinary pharmaceutical product innovation can improve the overall health and well-being of animals. [37].

4.1 Oral Modified-release Drug-delivery Systems

The preferred method for administering veterinary medications is oral delivery due to its low cost, non-invasive nature, minimal risk of infection, and painlessness. However, challenges exist in achieving stress-free administration and ensuring reliable bioavailability of the medication. In oral delivery, the drug is released from the formulation, dissolved in

gastrointestinal fluids, and absorbed into the body. Drug release from dose forms can be standard or customized to optimize drug delivery.

.

The key pharmacoeconomic concepts behind human-modified release medication delivery systems are: [17]:

1. Clinical effectiveness.
2. Reduced dosing's effectiveness (i.e.improved patient compliance).
3. Patient management (nursing or outpatient visits for repeat medicine delivery) and medical care savings (e.g. handling of adverse events or side effects).

Animal drug-delivery systems are developed to reduce animal handling, save costs, and minimize animal stress, especially in farmed animals. [14]. Consumer convenience and compliance are important drives for companion animals.

Most oral modified-release dose formulations fall into one of these categories [21]:

1. 1. Matrix: This drug delivery system involves embedding the drug within a polymer matrix, which gradually releases the drug as it breaks down in the gastrointestinal tract. However, the rate of drug release may be impacted by factors such as food and pH levels in the gastrointestinal tract.Reservoir system: A rate-limiting membrane surrounds the drug core in the dosage form. Food and GI pH may affect drug release from this system.
2. Osmotic system: Drug distribution uses osmotic pressure. This happens regardless of pH or other physiological conditions. This device can dispense drugs at a predetermined rate.

Another dosage form for modified oral release is gastric retention devices. Devices include:

- Floating systems: Multiparticulate drug-delivery methods like floating microspheres exhibit gastric retention for up to 12 h in humans. The medicine is slowly delivered from the microsphere's hollow inner core into the stomach. The stomach is emptied after drug release. Most studies show that retention of these systems is highly impacted by prandial state and that the device transits faster when taken fasting vs fed.
- Swelling system: The device swells and cannot leave via the pylorus. The dosage form is thus kept in the stomach. These systems' swelling rate and mechanical strength are crucial. Devices must be completely inflated before cleaning waves (i.e., achieve full swelling within 20 min or less). Although reliant on food, these systems may be kept in fed dogs' stomachs for more than 24 h.
- Bioadhesive systems: The technology delivers the medicine to a particular spot in the GI tract.
- Modified shape systems: Nondisintegrating polyethene or Silastic elastomer forms. Physiologically, the device's

size, shape, or flexibility keeps it in the stomach.

- High-density formulations: The tool dips in the stomach, slowing gastric emptying.

Some of these technologies might be used to give drugs to tiny animals. However, differences in stomach emptying rates across species could make this difficult.

4.2 Ophthalmic Modified-release Drug-delivery Systems

Traditional eye drops for medication delivery are not very effective due to the clearance processes, which result in the loss of most of the dose. To improve ocular medication absorption, innovative topical drug delivery technologies are being developed. These technologies include the use of solubility enhancers to raise drug concentrations in formulations, improving bioavailability, and the development of formulations that resist clearance, allowing more time for accumulation in ocular tissue. Additionally, drug penetration enhancers can be added to the formulation. Advanced drug delivery methods such as contact lenses, in situ gels, microemulsions, niosomes, liposomes, implants, microspheres, and micelles can allow for controlled release, reducing dosage frequency and the need for intrusive therapy, making it an effective option for chronic eye problems. (Fig,2).

In veterinary medicine, treating eye diseases in animals is challenging due to their different eye structures and physiology, cost, application challenges for owners, and flickering and lacrimation during administration that limits medicine absorption. Modified release ocular drug delivery methods, such as hydrogels or ointments, extend drug release, increase formulation contact, and reduce administrations. Mucoadhesives like gellan gum, poloxamers, cellulose, chitosan, and alginate enhance contact with the ocular surface, leading to extended ocular surface residency. However, blurred eyesight, inflamed lacrimal glands, and crusty eyelids are some of the disadvantages of using these methods.

(Silva, 2021).

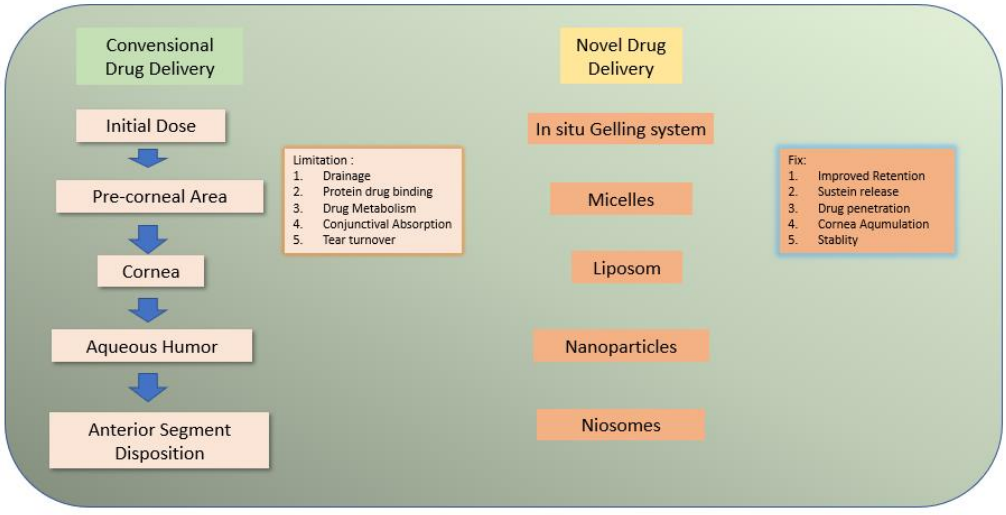

Fig 2. Comparison of conventional drug delivery and novel drug delivery system

Hydrogels are used to treat dry eyes in dogs and cats. This disease causes pain, visual impairments, tear film instability, and ocular surface damage. The treatment

uses 0.2% to 2% cyclosporine or 0.3% tacrolimus hydrogel. Artificial tears are made from many mimetic polymers such cellulose (Lacril®), hydroxypropyl guar (Sistan®), croscarmellose sodium (fresh-tear®, Lakrifilm®), polyvinyl alcohol (Tears® liquid film, Neo-Tears®), and hyaluronate (Hy-Drop®, Hylo-care®) [38].

4.3 Subcutaneous and Topical Modified-release Drug-delivery Systems

Drugs used against ectoparasites are the most frequently controlled or sustained release formulations, delivered subcutaneously or topically (fig. 3). Fleas, ticks, and ticks continually infest animals. Fipronil, methoprene, ivermectin, and permethrin treat and prevent ectoparasite infections. Ivermectin (IVM) has the most publications. IVM, a semisynthetic derivative of avermectin B1, manages internal and external parasites. Oral, topical, or subcutaneous administration is possible. Subcutaneous treatment is more effective than oral and topical in sheep, cattle, and goats; regarding the topical method, ivermectin sustain-release varnish's efficacy (SRV). The varnish contains IVM, amino methacrylate copolymer, and ethanol. Polymer and IVM remain when the varnish dries. Ivermectin's slow release reduces handling and medicine [38]

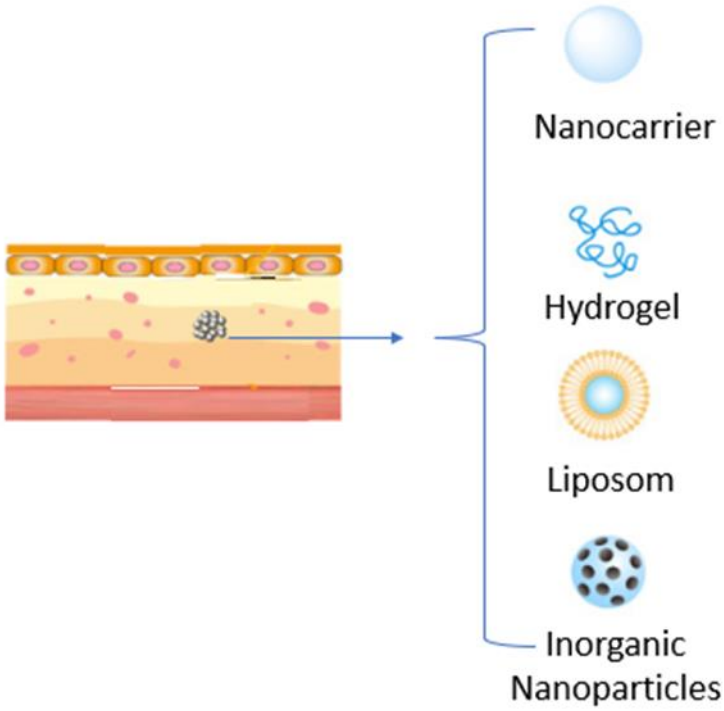

Fig 3.Various subcutan control release delivery system

4.4 Collars

Collars have been developed for preventing ticks, parasites, and mosquitoes in animals. The original collar technology by Shell involved a mix of vinyl resin and dichlorvos for tick prevention. Other drugs such as naled, sendran, rabon carbamate, and drug combinations have been added to these collars. The collar provides long-term delivery of up to 6 months and is easy to

administer to minimize animal stress. However, there are some downsides, including the delivery of large doses at the beginning, potential toxicity to animals, no indication of excess dosage, and potential skin sensitivities in animals. The combined medicament is included in the polymer matrix for this collar technology, with PVC, polyurethane, and ethylene-vinyl acetate being used for making the collars [38,39].

4.5 Injectable Modified-release Drug-delivery Systems

Many pet owners do not treat their pets orally, making injectable controlled release a preferred option. This is particularly challenging for cats, who may go without food for days. Infections often require multiple days of treatment. Injectable pharmaceuticals must meet high-quality standards. Various formulations, such as dispersions, aqueous solutions, oily injections, suspensions, sediment-in-place suspensions, microspheres, and durable nanoparticles have been developed for injectable administration to improve targeted therapy, reduce dosage, and increase bioavailability while maintaining animal welfare [38,40].

5. Conclusion

The drug delivery route system consists of oral, topical (transdermal, ocular), and parenteral (subcutaneous, intravenous, intramuscular). Things that need to be considered in determining the route of drug delivery in animals are gender, metabolic system, animal anatomy and physiology, and drug characteristics. New drug delivery systems in the veterinary field will be beneficial to adjust the bioavailability of drugs for specific animals, thus would reduce the number of doses, owner stress, and duration of treatment. Such systems include subcutaneous implant systems, injection-controlled release systems, topical creams that can be placed on the ears, eye and mouth inserts, and vaginal inserts.

References

1. Cerbu, C.; Kah, M.; White, J.C.; Astete, C.E.; Sabliov, C.M. Fate of Biodegradable Engineered Nanoparticles Used in Veterinary Medicine as Delivery Systems from a One Health Perspective. Molecules 2021, 26, doi:10.3390/molecules26030523..
2. Adepu, S.; Ramakrishna, S. Controlled drug delivery systems: Current status and future directions. Molecules 2021, 26, doi:10.3390/molecules26195905.
3. Brayden, D.J. Novel drug delivery strategies in veterinary medicine. Ir. Vet. J. 2003, 56, 310–316.
4. Lavy, E.; Kirmayer, D.; Nudelman, Z.; Orenshtein-Vilensky, L.; Rowan, T.G.; Shenderovich-Gefter, J.; Friedman, M. Aspects in controlled drug delivery for topical applications in veterinary medicine. Vet. Anim. Sci. 2022, 15, 100235, doi:10.1016/j.vas.2022.100235.
5. Finka, L.R. Conspecific and Human Sociality in the Domestic Cat: Consideration of Proximate Mechanisms, Human Selection and Implications for Cat Welfare. Animals 2022, 12, doi:10.3390/ani12030298.
6. Herdiana, Y.; Wathoni, N.; Sriwidodo; Adnyane, I.K.M. Veterinary Drug Development from Indonesian Herbal Origin: Challenges and Opportunities. Indo J Pharm 2021, 3, 26–37, doi:10.1017/CBO9781107415324.004.
7. Izabela Wierzbowska, Sławomir Kornás, A.P. and K.R. The Prevalence of Endoparasites of Free Ranging Cats. Animals 2020, 1–13.
8. Mohebali, M.; Zarei, Z.; Khanaliha, K.; Kia, E.B.; Motavalli-Haghi, A.;

Davoodi, J.; Tarighi, F.; Khodabakhsh, M.; Rezaeian, M. Intestinal protozoa in domestic cats (Carnivora: Felidae, felis catus) in northwestern iran: A cross-sectional study with prevalent of microsporidian and coccidian parasites. Iran. J. Parasitol. 2019, 14, 136–142, doi:10.18502/ijpa.v14i1.728.

9. Hernandez, E.; Fawcett, A.; Brouwer, E.; Rau, J.; Turner, P. V. Speaking up: Veterinary ethical responsibilities and animalwelfare issues in everyday practice. Animals 2018, 8, 1–22, doi:10.3390/ani8010015.
10. Mora, C.; McKenzie, T.; Gaw, I.M.; Dean, J.M.; von Hammerstein, H.; Knudson, T.A.; Setter, R.O.; Smith, C.Z.; Webster, K.M.; Patz, J.A.; et al. Over half of known human pathogenic diseases can be aggravated by climate change. Nat. Clim. Chang. 2022, 12, doi:10.1038/s41558-022-01426-1.
11. Agrebi, S.; Larbi, A. Use of artificial intelligence in infectious diseases. Artif. Intell. Precis. Heal. 2020, 415–438, doi:10.1016/b978-0-12-817133-2.00018-5.
12. Rehme, T.; Hartmann, K.; Truyen, U.; Zablotski, Y.; Bergmann, M. Feline Panleukopenia Outbreaks and Risk Factors in Cats in Animal Shelters. Viruses 2022, 14, 15–17, doi:10.3390/v14061248.
13. Priambudi, M.Z.D.R.; Haskito, A.E.P.; Inayah, K.; Adrenalin, S.L. Detection of feline panleukopenia with antigen test kit. ARSHI Vet. Lett. 2022, 6, 3–4, doi:10.29244/avl.6.1.3-4.
14. Endris, M.; Feki, E.; Endris, M. Review on Effect of Stress on Animal Productivity and Response of Animal to Stressors Review on Effect of Stress on Animal Productivity and Response of Animal to Stressors. J. Anim. Vet. Adv. 2021, 20, 1–14, doi:10.36478/javaa.2021.1.14..
15. Hofmann-Lehmann, R.; Hosie, M.J.; Hartmann, K.; Egberink, H.; Truyen, U.; Tasker, S.; Belák, S.; Boucraut-Baralon, C.; Frymus, T.; Lloret, A.; et al. Calicivirus Infection in Cats. Viruses 2022, 14, 1–31, doi:10.3390/v14050937.
16. Andriani, M.D.; Mihardi, A.P.; Pakpahan, S.N.; Sovinar, M. KIVSA-6 Stomatitis Kompleks pada Seekor Anak Kucing. Hemera Zoa 2018, 314–315.
17. Yousuf, J.; Bhat, R.A.; Dar, S.H.; Shafi, A.; Irshad, S.; Yatoo, M.I.; Parrah, J.U.; Muhee, A.; Mir, A.Q. A review on the diagnosis of feline infectious peritonitis. Appl. Vet. Res. 2022, 1, 1–5, doi:10.31893/avr.2022005.
18. Moroni, B.; Rossi, L.; Bernigaud, C.; Guillot, J. Zoonotic Episodes of Scabies: A Global Overview. Pathogens 2022, 11, doi:10.3390/pathogens11020213.
19. Colombo, M.; Morelli, S.; Sacra, M.; Trezza, G.; Paoletti, B.; Traversa, D.; Cesare, A. Di An Uncommon and Severe Clinical Case of Sarcoptes scabiei Infestation in a Cat. 2023, 0–5.
20. Bradley, A.E.; Wancket, L.M.; Rinke, M.; Gruebbel, M.M.; Saladino, B.H.; Schafer, K.; Katsuta, O.; Garcia, B.; Chanut, F.; Hughes, K.; et al. International harmonization of nomenclature and diagnostic criteria (INHAND): Nonproliferative and proliferative lesions of the Rabbit. J. Toxicol. Pathol. 2021, 34, 183S-292S, doi:10.1293/tox.34.183S.
21. Kraabøl, M.; Gundersen, V.; Fangel, K.; Olstad, K. The taxonomy, life cycle and pathology of sarcoptes scabiei and notoedres cati (Acarina, sarcoptidae): A review in a fennoscandian wildlife perspective. Fauna Nor. 2015, 35, 21–33, doi:10.5324/fn.v35i0.1652.
22. Indarjulianto, S.; Yanuartono, Y.; Widyarini, S.; Raharjo, S.; Purnamaningsih, H.; Nururrozi, A.; Haribowo, N.; Jainudin, H.A. Infeksi Microsporum canis pada Kucing Penderita Dermatitis (MICROSPORUM CANIS INFECTION IN DERMATITIS CATS). J. Vet. 2017, 18, 207, doi:10.19087/jveteriner.2017.18.2.207.
23. Kottferová, L.; Molnár, L.; Čonková, E.; Major, P.; Sesztáková, E.; Szarková, A.; Slivková, M.; Kottferová, J. Fungal Flora in Asymptomatic Pet Guinea Pigs and Rabbits. Animals 2022, 12, 1–10, doi:10.3390/ani12182387.

24. Ganguly, S.; Sharma, V. Dermatophytosis in animals: an overview. Pharm. Biol. Eval. 2017, 4, 66, doi:10.26510/2394-0859.pbe.2017.10.
25. Clements, A.C.A.; Addis Alene, K. Global distribution of human hookworm species and differences in their morbidity effects: a systematic review. The Lancet Microbe 2022, 3, e72–e79, doi:10.1016/S2666-5247(21)00181-6.
26. Silalahi, G.E.; Tjahajati, I.; Nugroho, W.S. Survei Helminthiasis pada Anjing di Wilayah Daerah Istimewa Yogyakarta. 2022, 49–53.
27. Alba-Hurtado, F.; Muñoz-Guzmán, M.A. Toxocariosis: From a One Health Perspective. In; Morales-Montor, J., Río-Araiza, V.H. Del, Hernandéz-Bello, R., Eds.; IntechOpen: Rijeka, 2022; p. Ch. 10 ISBN 978-1-80355-568-3.
28. Phoosangwalthong, P.; Luong, N.H.; Wongwigkan, J.; Kamyingkird, K.; Phasuk, J.; Pattanatanang, K.; Thammasonthijarern, N.; Kengradomkij, C.; Chimnoi, W.; Odermatt, P.; et al. Toxocara canis and Toxocara cati in Stray Dogs and Cats in Bangkok, Thailand: Molecular Prevalence and Risk Factors. Parasitologia 2022, 2, 88–94, doi:10.3390/parasitologia2020009.
29. Xenoulis, P.G.; Fracassi, F. Feline Comorbidities: Clinical perspective on diabetes mellitus and pancreatitis. J. Feline Med. Surg. 2022, 24, 651–661, doi:10.1177/1098612X221106355.
30. Rosca Burlacu, M.; Solcan, G. Feline Diabetes Mellitus and Differential Diagnosis We Need to Consider. Bull. Univ. Agric. Sci. Vet. Med. Cluj-Napoca. Vet. Med. 2015, 72, doi:10.15835/buasvmcn-vm:11329.
31. Gottlieb, S.; Rand, J. Managing feline diabetes: current perspectives. Vet. Med. Res. Reports 2018, Volume 9, 33–42, doi:10.2147/vmrr.s125619.
32. Pérez-Enriquez, J.M.; Romero-Romero, L.; Alonso-Morales, R.A.; Fuentes-Pananá, E.M. Tumor prevalence in cats: experience from a reference diagnostic center in Mexico City (2006-2018). Vet. México OA 2020, 7, doi:10.22201/fmvz.24486760e.2020.4.837.
33. Ludwig, L.; Dobromylskyj, M.; Wood, G.A.; van der Weyden, L. Feline Oncogenomics: What Do We Know about the Genetics of Cancer in Domestic Cats? Vet. Sci. 2022, 9, doi:10.3390/vetsci9100547.
34. Czajkowski, P.S.; Parry, N.M.; Wood, C.A.; Casale, S.A.; Phipps, W.E.; Mahoney, J.A.; Spector, D.I.; Price, L.L.; Berg, J. Outcome and Prognostic Factors in Cats Undergoing Resection of Intestinal Adenocarcinomas: 58 Cases (2008–2020). Front. Vet. Sci. 2022, 9, 1–7, doi:10.3389/fvets.2022.911666.
35. Ozgunay, S.; Murray, J.K.; Rowe, E.; Gee, N.R.; Bartholomeus, M.; Casey, R. Cognitive and Composite Behavioural Welfare Assessments of Pet Cats between the Ages of 9–22 Months, Living in Single and Multi-Cat Households. Animals 2021, 11, 1–17..
36. Monteiro, B.P.; Lascelles, B.D.X.; Murrell, J.; Robertson, S.; Steagall, P.V.M.; Wright, B. 2022 WSAVA guidelines for the recognition, assessment and treatment of pain. J. Small Anim. Pract. 2022, n/a, doi:https://doi.org/10.1111/jsap.13566.
37. Santis, F. De; Boari, A.; Dondi, F.; Crisi, P.E. Drug-Dosing Adjustment in Dogs and Cats with Chronic Kidney Disease. Anim. 2017, 12, 1015–1023.
38. da Silva, C.F.; Almeida, T.; de Melo Barbosa, R.; Cardoso, J.C.; Morsink, M.; Souto, E.B.; Severino, P. New Trends in Drug Delivery Systems for Veterinary Applications. Pharm. Nanotechnol. 2020, 9, 15–25, doi:10.2174/2211738508666200613214548.
39. Lavy, E.; Kirmayer, D.; Nudelman, Z.; Orenshtein-vilensky, L.; Rowan, T.G.; Shenderovich-gefter, J.; Friedman, M. Aspects in controlled drug delivery for topical applications in veterinary medicine. Vet. Anim. Sci. 2022, 15, 100235, doi:10.1016/j.vas.2022.100235.

40. Carvalho, S.G.; Silvestre, A.L.P.; Martins dos Santos, A.; Fonseca-Santos, B.; Rodrigues, W.D.; Palmira Daflon Gremião, M.; Chorilli, M.; Villanova, J.C.O. Polymeric-based drug delivery systems for veterinary use: State of the art. Int. J. Pharm. 2021, 604, 120756, doi:https://doi.org/10.1016/j.ijpharm.2021.120756.