VETERINARY DOSAGE FORMS: REVIEW

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ABSTRACT

Veterinary medicine is the branch of science that deals with the application of medical, surgical, public health, dental, diagnostic and therapeutic principles to nonhuman animals including wildlife and domesticated animal including livestock working animals and companion animals. Veterinary dosage forms show great promise for the future of diagnostics, drug therapies, and biotechnologies. In this review, the attention is focused to give brief information regarding classification of animals, need of veterinary dosage forms, flavors used in animals, different routes of administration and dosage form in animals. Stability study and Controlling Authorities by various countries has been briefly discussed which give focus on regulatory requirements of Veterinary Products.

Keywords: Veterinary dosage forms, Veterinary devices, Animals

INTRODUCTION[1,2]

Veterinary medicine is the branch of science that deals with the application of medical, surgical, public health, dental, diagnostic and therapeutic principles to nonhuman animals including wildlife and domesticated animal including livestock working animals and companion animals. Just like humans, animals receive medicines to keep them healthy. Drugs have been compounded for veterinary practice for many years, but, Regulations and Compliance Policy Guidelines (CPGs) should be recognized. A CPG issued in July 2003 listed the current Food and Drug Administration (FDA) limitations on compounding for veterinary medicine. However, veterinarians and pharmacists must be aware of potential incompatibilities and practices that may interfere with the drug’s stability, purity, and/or potency.

Animals provide us with companionship (e.g. Dog and cat), recreation (e.g. Horse), food (e.g. Cattle and pig), and manual labor (whether an elephant carrying logs in Thailand or a hunting dog retrieving a downed pheasant in South Dakota). Just like humans, these animals have received medicines to keep them healthy, and the reasons for producing single-dose veterinary dosage forms are the same as those in humans; to permit delivery of an active in a form that is effective, safe, and able to be handled and administered by the end user. However, when one extends that to long-acting dosage forms, the reasons for developing such a system differ between humans and animals. In the case of humans, the reasons for developing a drug into a long-acting delivery system is to minimize animal handling to reduce the stress to animals from repeated administration and to reduce the cost of treatment in terms of money and time spent by the end user on drug administration. These reasons do not impact on the science used to develop such dosage forms, but they do impact heavily on the outcomes such as the size, shape, volume administered etc. of the dosage form.

Veterinary pharmaceuticals play an important role in human and animal health. Although some dosage forms are specially designed for use in animals (e.g. Ear tags, collars and darts), most drug delivery systems (including nano-carriers and controlled drug delivery systems) are common among animals and human. A successful drug development process (for human or animal use), from initial drug discovery. Market, requires skill and knowledge in different areas of science of which some disciplines (e.g. Pharmaceutics) are exclusively covered in pharmacy undergraduate or postgraduate programs. Pharmaceutics is the art, science and technology of drug delivery system design, manufacture and control and include formulation studies, dosage form design, pharmaceutical processing, quality control, quality assurance, biopharmaceutics and etc. Therefore, like human medicine, pharmacists are expected to design, manufacture and control veterinary drug delivery systems at both levels of pharmaceutical companies or compounding in a pharmacy. This is not what is happening in most veterinary pharmaceutical companies and almost all veterinary-based pharmacies in here, where the professions are performed by veterinary medical doctors (Doctor of Veterinary Medicine, DVM). The educational program in veterinary medicine (DVM) is clinically-based and is focused on prevention, diagnosis and treatment of animal diseases, the same perspective as that designed for the physicians (MD). There is not such authorization for physicians to act the same in human-oriented pharmaceutical systems. On the other hand, formulation of many drugs for human use is seldom suited for animal administration. Design and preparation of veterinary drug delivery systems require different considerations and is facing more challenges than that of human formulations and cannot be implemented based on human data only. Following are some special considerations.

Classification of animals

1) Classification based upon eating habit
   - Herbivorous species consist of horse and ruminant animals like cattle, sheep and goat.
   - Carnivorous species consist of dog and cat.
   - Omnivorous species consist of pig.
   - The digestive system is the principal distinguishing feature between herbivorous and carnivorous species.
   - Humans and animals having distinguishing digestive system main difference in the length of the intestinal tract.

2) Classification based upon the runnen
   Hofmann and Stewart divided ruminants into three major categories based on their feed type and feeding habits:
   - Concentrate selectors
   - Intermediate types
   - Grass or roughage eaters
   - pseudo-ruminants

3) Canine, feline
   They are classified into four types
   - Foxes
   - Wolves
Need of veterinary dosage forms
Veterinary science is vital to the study and protection of animal production practices, herd health, and monitoring spread of disease like swine flu, chikungunya etc.

Flavors that animals prefer include
Dog prefers Beef, Chicken, Cheddar Cheese, Molasses, Peanut Butter, Liver, Raspberry, Strawberry.
Cat prefers Tuna, Chicken, Beef, Cheddar Cheese, Peanut Butter, Liver, Butterscotch.
Bird prefers Grape, Mandarin Orange, Tutti-frutti, Molasses, Pina Colada.
Horse prefers Apple, Creamy Caramel, Molasses, Licorice, Cherry.
Rabbit prefers Banana
Ferret prefers Bubble Gum, Molasses.
Gerbils prefers Mandarin Orange, Tutti-frutti.

Diseases in animals
1) Parasitic diseases
Strongyloidea (Swine)
Ancylostomatoidea (Horse)
Siphonaptera (Cattles)
Ascaridoidea (Cats and dogs)
2) Bacterial diseases
Yersiniosis (Swines)
Salmonellosis (Chickens)
Q-fever (Cattles)
Rabies (Dogs)
3) Diseases transmitted from animals to human
These are called as Zoonotic diseases. All infectious diseases can transmit from animals. Example of zoonotic diseases includes—Plague, Rabies, Lyme diseases, Ringworm, Tick paralysis, Swine flu, Giardiasis, Chickengunia.

Some pharmacological agents that are used exclusively in animals
1) Xylazine: sedative, analgesic
2) Yohimbine: xylazine reversal
3) Detomidine: preanaesthetic medication
4) Atepamezole: Detomidine reversal
5) Acepromazine: preanaesthetic medication
6) Etorphine: neurpleptanalgesia
7) Diprenorphin: etorphin reversal
8) Flunixin: anti-inflammatory
9) Droperidol: neurpleptanalgesia
10) Azeperone: preanaesthetic medication

CLASSIFICATION OF VETERINARY DELIVERY DEVICES [3,4,5]
Because of the variety of dosage forms in veterinary medicine and the diversity of animal and bird species treated, drug or dosage delivery sometimes requires the development of specific devices to ensure fast, safe, effective and low-cost efficient treatment.

There are basically two types of devices
1. Those used to administer the dosage form to the animal. E.g. Balling guns, syringes, implants etc.
2. Those which meter drug from its site of implantation, insertion, ingestion or attachment to the animal over a potentially long period of time.
1. Oral devices
   a. Balling guns
   b. Esophageal delivery devices
   c. Drench syringes
   d. Liquid drench guns
e. Powder drench guns
f. Paste dispensers
g. Water medication metering devices
h. Rumen lodging devices
i. Hollow bits
j. Non pyloric passage devices
k. Miscellaneous oral dose dispensers
l. Buyoant devices
m. Prolonged release devices
n. Miscellaneous oral dose dispensers
a. Balling guns
It is not easy to push a pill down or other medication a large animal’s throat. For that purpose, veterinarians use balling guns. The balling gun is commonly used on cattle, horses, pigs, sheep, and goats. It consists of a tube with a holder for the medication, usually a capsule, at one end. Veterinarians push the plunger on the end of the tube to force the medication into the animal. Balling guns come in various sizes depending on the species. Balling guns are simple devices used for oral administration of bolus to animals. It is a tube with a capsule holder on one end. These do not deliver devices can be classified broadly as a single or multiple dose. Single dose balling guns are designed to accommodate a number of bolus sizes. Multiple balling guns can be loaded with one or several boluses of the same size. The boluses are held in the barrel usually by a flexible constricting at the barrel tip. Bolus delivery, which is based upon distance of plunger travel in the barrel, can be adjusted to deliver one or several boluses sequentially. Balling guns are used for solid dosage administration for calves. Beef cattle, dairy cattle, lambs, sheep, foals, horses, dogs, cats etc. While use the bolus is placed in the balling gun cup or barrel and with the animal’s head immobilized, the tube is passed along the midline of the mouth over the base of the tongue. The tongue may have to be pulled out if it obstructs the tube. When the animal swallows, the tube is pushed gently into the gullet, the handle is squeezed, and the bolus is gently expelled.

Fig. 1: Balling gun
Importance of Oral route
1. Improved clinical effectiveness.
2. The relative efficiency of reduced dosing regimens (i.e. improved animal patient compliance).
3. Relative savings in animal patient handling and medical care.
4. Convenience and compliance are major drivers for companion animals.

a. Esophageal delivery devices
Direct administration of the dosage form to the stomach of an animal has a number of advantages:

i. Dosage administration is more efficient and professional.
ii. The total dose gets into the stomach.
iii. Irritating substances can be administered that might otherwise cause esophageal or pharyngeal lesions, i.e. Carbon disulfide and chloral hydrate can be administered without danger.
iv. Feed, water, and medication can be delivered to animals that are unable or refuse to eat, or should not eat because of pharyngeal or esophageal lesions.

Devices used for esophageal administration of medication are of two types:

i. Syringes
ii. Tubes

Syringes - Two types of syringes are available. The first type of syringe is 'Regular dosing syringes' can be adapted for direct stomach delivery by attaching any of a series of dose pipes. The second type of syringe is a 'Dose pipe'. The syringe barrel is passed through the esophagus to the stomach.

Fig. 2: Syringe

Tubes
Syringes, injections, pumps and funnels may be used to deliver the medication to an esophageal tube which is inserted into the stomach through a speculum either in the mouth or a nostril.

Fig. 3: Tube
Source: http://www.bestforbreeder.com

b. Drench syringes
The drench syringe can either have a preset volume or be an adjustable hypodrench designed to deliver the desired volume of the solution or suspension to the gullet. The preset volume syringe can be either all metal ranging in size from 2 to 320Z.

Fig. 4: Drench syringe
Source: http://hambydairysupply.com

c. Liquid drench guns
Drenching guns provide an easy, relatively fast means of orally administering solutions or suspensions of either an aqueous or oily nature.

Fig. 5: Liquid drench gun
Source: http://hambydairysupply.com

Liquid drench guns are of three types:

1. Single dose gun
2. Multi dose drench gun
3. Automatic drench gun

1. Single dose gun: This syringe gun is primarily designed for large volume distribution. It is filled by pushing the piston to the end of its stroke and then drawing it back after dipping the end into the liquid to be injected. The free end of the tube is then introduced into the mouth of the animal.

2. Multi dose drench gun: This gun is used to administer doses of drench in step quantities.

3. Automatic drench gun: Automatic drench guns are so designed that the chamber refills directly after injection from a large volume reservoir which is usually strapped to the operators back. For example May and Baker Ltd. Manufacture a worm drench for cattle, sheep and goats which require no addition of water, mixing or transfer of drench solution to carry packs.

d. Powder drench guns
Drenching of large animals with a powder formulation can be achieved using powder drench guns. To use of these guns the required amount of powder poured into the barrel and inserted in the mouth, the trigger is pulled and powder sprays in the mouth.

Fig. 6: Powder drench gun
Source: www.thefarmstore.com
f. Paste Dispensers

Paste formulation for oral administration to animals may be delivered by:

- Paste guns
- Paste syringes
- Squeeze tubes

![Fig. 7: Paste dispenser](http://www.bestforbreeder.com)

- Paste guns In a study conducted by Ray and Brown, 175 weaned calves were used to measure different dosage forms of anthelmintics: paste, bolus, injections and drench.

- Paste syringes- Syringes can be designed to deliver one single dose which can be varied according to the weight of the animal or they can be set to deliver a limited number of multiple dose paste boluses.

- Squeeze bottles or Tubes- Pet Kalorie by Hoover-Lockhart, Shawnee, Kanas is a high calorie dietary supplement in paste form used to treat malnutrition in piglets.

g. Water medication metering devices

The medications formulated as:

- Dry powders for reconstitution

![Fig. 8: Water medication metering device](http://www.fatcow.com.au/t/Animal-Medical-Supplies)

- Concentrated solutions

Unhealthy animals allow to drink water continuously. Water as medium for drug solubility and quick absorption. Concentration of drugs in water to be half only, this problem may overcome by its limited solubility. In addition, the dry powders are usually formulated with sugar as lactose or dextrose.

The use of these may cause a build-up of bacteria and fungi in water lines. The drug stability in water must be stated on the label. The powder medication was dissolved at the time of administration into water to make a stock solution. Medication of a large number of animals or birds can be accomplished by adding regulated amounts of the soluble drug to their drinking water. Medicaments, vaccines, Wormers, electrolytes, disinfectants and antibiotic surfactants are dosed in this fashion. The drug concentration in water is half of that in the field as the animals drink twice as much water as they consume feed. Water medication metering devices are falling into two categories:

1. In line
2. Trough

h. Rumen lodging devices

In ruminant animals rumen acts as drug loading site for prolonged release.

![Fig. 10: Non pyloric passage devices](http://www.thefarmstore.com)

<table>
<thead>
<tr>
<th>Medication type</th>
<th>Duration of action</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthelmintics</td>
<td>12 months</td>
<td>Piperazine phosphate</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>1 week</td>
<td>Penicillins, tetracyclines</td>
</tr>
<tr>
<td>Antibloat agent</td>
<td>6 weeks</td>
<td>Silicons</td>
</tr>
<tr>
<td>Growth stimulants</td>
<td>3 months</td>
<td>Stilbesterol</td>
</tr>
<tr>
<td>Sulfonamides</td>
<td>1 week</td>
<td>Sulfadiazine</td>
</tr>
<tr>
<td>Systemic insecticides</td>
<td>6 months</td>
<td>Organophosphorus compounds</td>
</tr>
<tr>
<td>Trace elements</td>
<td>-</td>
<td>Co, cu, Mn, Mb</td>
</tr>
</tbody>
</table>

i. Hollow bits- It is useful in horses. Heat from the horse’s mouth and salivary action gradually elute active ingredient through perforations in the hollow bit. The active ingredient is incorporated in a compartment in the bit in the form of a confection.

![Fig. 9: Hollow bits](http://www.thefarmstore.com)

j. Non pyloric passage devices: Device can be retained in animal stomachs for an extended period of time if it is larger than the pyloric opening. However, because the diameter of the pylorus differs between and among animal species and because the device may be of quite large dimensions and therefore difficult to swallow.
k. Miscellaneous oral dose dispensers

It includes

- **Pump type dispensers**
- **Nursers**
- **Droppers**
- **Mineral dispensers**
- **Mouthpieces**

**Pump type dispensers** - Simple ball valve operated dispensers generally designed to deliver 1ml have been used for oral administration of solutions, suspensions and emulsions to small animals. Example - administration of antibiotics to piglets.

**Nursers** - Nurse consisting of a 2 fluid Oz plastic bottle with a specially designed nipple. Drug formulations including solutions, suspensions or emulsions can be added to the nursing solution and thus provide easy, nontraumatic delivery to small animals.

**Droppers** - For the dose of 1 ml or less, calibrated droppers are available. The solution should be dispensed from graduating volume indicators on the dropper tube.

**Mineral dispensers** - Sturdibox, TUCO Chemical company is a device for the delivery of mineral mixes. It is constructed of concrete and permits the presentation of the mineral mixers in the yard, pen or pasture.

**Mouth Pieces** - Effective oral dosing of solutions may require the design of specialized dose pipes or mouth pieces to ensure that all the liquid being dosed passes down the animal’s throat and that the animal can easily be handled. One device is a U-shaped conduit.

I. Buoyant devices

This can be designed by

- The density of the formulation allows the drug to float on the stomach gastric fluid.
- Interaction between the gastric fluid and foaming agents.

m. Prolonged release devices

Sustained delivery of the formulations can be established by this device. Prolonged release devices are of three types

- **Erodible devices**
- **Matrix devices**
- **Membrane devices**

2. Topical devices

a. **Pour on, spot on application**
b. **Dust bags**
c. **Spray race and dip**
d. **Teat dip**
e. **Aerosol Dispensers**
f. **Flea and tick collars**
g. **Percutaneous devices**

a. **Pour on, spot on application**

These formulations contain organophosphorus insecticides or anthelmintic dissolved in organic solvents as DMSO or aromatic hydrocarbons.

The advantages of these formulations are

1. Elimination of risk of trauma and damage at injection site
2. No special skills are required for the application
3. Sterile preparations are not necessary
4. Troublesome animals are dosed easily
5. Speed of treatment is quick.

![Fig. 11: Pour on, spot on the application](http://tickapp.tamu.edu/control.php)

**Source**: http://tickapp.tamu.edu/control.php

b. **Dust bags**

Cattle are treated with insecticide, powders through those of a device called as Dustbag. Dosing accomplished by animals brushing against the bag as they walk beside or under it. This bag has an inner porous storage bag containing the insecticide dust formulation Forced–use bags are hung in doorways or tree or pole.

![Fig. 12: Dust bags](www.animalsupply.com)

**Source**: www.animalsupply.com

C. **Spray race and dip**

For control of ectoparasites in economic animals, dipping is an extensively used method. A dip formulation containing the drug is diluted in a large dipping bath through which the animal is driven. This path must be long, wide, and deep enough to cause immersion of the animal. It must be non toxic to the animal, but toxic to ectoparasites.

![Fig. 13: Spray race and dip](http://www.butox-info.com/butox/applications.asp)

**Source**: http://www.butox-info.com/butox/applications.asp
d. Aerosol Dispensers

Aerosol dispensers provide a number of advantages:

1. The medication is delivered directly to the affected area in a desired form such as a spray, stream, quick break foam or stable foam.
2. The medicament is applied without mechanical irritation to the sensitive area.
3. A dose can be delivered without contaminating the remaining material.

![Aerosol dispensers](http://www.bombayharbor.com/Product/10972/Automatic-Aerosol-Dispenser.html)

**Fig. 14: Aerosol dispensers**


e. Flea and tick collars

There are two types of flea and tick collars:

1. Vaporous
2. Powder producing collars

Both contain the insecticide and a plasticized solid thermoplastic resin.

**Vaporous collar** contains relatively high vapor pressure liquid pesticide mixed throughout the collar. The pesticide is slowly released and fills the atmosphere adjacent to the animal, that kills the pest but innocuous to the animal.

**The powder producing** collar contains a solid solution of the drug in the resin.

Shortly after the collar is processed the particles migrate from within the body of resin and form a coating of particles known as a bloom. Ticks and fleas migrate through the neck area of the animal as they contact the active pesticide is released and kills the pest.

![Flea and tick collars](http://www.atechdesigns.com)

**Fig. 16: Percutaneous devices**

Source: [http://www.atechdesigns.com](http://www.atechdesigns.com)

f. Percutaneous devices

1) Topical reservoir

Controlled percutaneous absorption of an active drug moiety from a depot device attached to the skin of an animal would ensure a constant, easily terminated, prophylactic drug delivery over a period of hours, days, weeks or months.

2) Ear tampon

It consist of cylindrical resilient absorbing materials placed in the ear cavity of animals used to deliver Growth stimulating hormones, corticosteroids, antibiotics and other medicaments for prolonged periods of time.

3. Parenteral devices

- Single dose syringe

Syringes are used to express the hydrated OTC Tree Injection Formula through the back of the Valve and into the palm.

![Single dose syringe](http://store.palmtreesaver.com)

**Fig. 17: single dose syringe**

Source: [http://store.palmtreesaver.com](http://store.palmtreesaver.com)

- Multiple dose syringes

Multi-dose syringes for use in breeding stock.

![Multiple dose syringes](http://store.palmtreesaver.com)

**Fig. 18: Multiple dose syringes**

Source: [http://store.palmtreesaver.com](http://store.palmtreesaver.com)

- Automatic syringes

The vial holder model of this automatic syringe is often used for vaccination or injection of swine.

![Automatic syringe](http://www.nechmad.com)

**Fig. 19: Automatic syringe**

Source: [http://www.nechmad.com](http://www.nechmad.com)

- Multi compartment syringes

Multi-compartment syringe for storing two or more substances in separate compartments.
• **Pole mounted syringe** Used for remote administration of medicaments. Long needles are used which are secured on housing that supports the needle to prevent its breakage.

• **Mastitis syringes** Drug formulation can be delivered to the site of infection in a cow with mastitis. Needles can be inserted directly into the mammary gland through the teat canal.

• **Jet injectors**- Dose of liquid medicaments is expelled under extremely high pressure against epidermis of the animals. Used to vaccinate a large number of animals and birds.

• **Projectile delivery system**- Used to deliver drug parenterally from a distance.

• **Implanting devices**

  Three types of Implanting devices are used in veterinary practices:

  - Pellet Implanting devices
  - Ball Implanting devices
  - Molten Implanting devices

  This Feeding System is a convenient and versatile system providing a method to feed multiple animals simultaneously, making it ideal for multiple animal feeding studies or other applications which require precise parallel pumping. The standard syringe rack can hold up to 10 syringes ranging in size from 50cc to 140cc. You can use plastic or glass syringes. Other syringes sizes may be used. The Broad performance characteristics of the Feeding System make it ideal for small drug or large volume nutritional variables on large animal populations.

  - High pressure
  - Large flow rate range
  - High reliability
  - High accuracy and precision

**Implants:** These are generally smaller and are designed to implant beneath the surface of the skin subcutaneously or intramuscularly

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Vaginal drug dispenser- Used for synchronization of estrus. Synchronization will increase productivity. E.g. flurogestone acetate, medroxy progesterone acetate as sponge.

**Miscellaneous syringes**

It includes:

- Gas powdered hypodermic syringe
- Motor actuated syringe
- Flexible needle syringe

1. **Nasal devices**

   Used for delivery of vaccines as solutions or powders.

   It includes:

   i. Automatic single or multiple dose syringe
   ii. Single dose dropper vial
   iii. Spray dispensers
   iv. Powder mist dispensers

**The basis for selecting a dosage form**

- Comparative physiology of digestive system
- Species difference in drug distribution and rate of elimination
- Skin type
- Endocrinology
- Respiration
- Behavior
- Species comparison using pharmacokinetics concept

**FORMULATION OF DRUG DOSAGE FORMS OF ANIMALS**

**Dosage forms**

A. **Rationale**

B. **Solid dosage forms**

C. **Oral liquid dosage forms**

D. **Parenteral dosage forms**

E. **Mastitis products**

F. **Pastes**

G. **Pellets implants**

H. **Model dosage forms**

A. **Rationale**

The dosage form is a vehicle containing a drug, custom made from a compound with specific chemical and physical characteristics.

B. **Solid dosage forms**

i. **Tablet and boluses**

Solid dosage forms are less popular for animals because the administration of solid dosage forms can be time consuming and uncertain. A dog or cat may not readily accept the tablet and one is forced to hide the tablet in the food. The animal will be dosed on the basis of weight, the amount of drug given to a large animal such as a cow may be considerable. For drugs such as the sulfonamides, which are dosed at relatively high rates.

Capsule shaped or cylindrical shaped tablet called a Bolus. The instrument used to hold the bolus and drop into the animal’s mouth is called a balling gun. These are less popular for animals because of their administration may be time consuming, hazardous, uncertain in tablet swallowing, and they may spit out or dropped from the mouth. This can be overcome by use of acceptable odors, flavors,
sweeteners. Drugs are given on the basis of weight or body surface area. The labeling of solid dosage forms, must be stated in mg or g per kg of body weight. A special tablet BOLUSE is commonly used to provide larger doses; it can range from 3 to 16 mg in weight. Boluses are capsule shaped or cylindrical. Boluses are administered by an apparatus called bailing gun, consisting of a barrel with a plunger that can hold one or more boluses. The tube inserted into the animal’s mouth over the base of the tongue and such animal swallows the plunger is depressed. The bolus is expelled into the gullet of the animal, after it swallowed by reflex. Bolus formulation poses challenges because of the high to excipients ratio. Less room left for diluents, binders and other additives. Cattle or sheep possible to utilize the concept of long acting boluses, which stays in GIT more than 12 hrs. The density is the critical factor to maintain the retention.

ii. Long acting boluses
One of the factors limiting the duration of an orally administered drug in humans is the time of transit through the gastrointestinal tract.

C. Oral liquid dosage forms
1) Solutions and suspensions
Solutions are the simplest and probably most economical liquid dosage forms for oral use is an aqueous solution. For increasing the water solubility of solutions addition of alcohol, propylene glycol, glycerin, dimethy1 sulfoxide. Edible vegetable oils can also be used to prepare a solution of a drug for oral use.

Suspensions are viable alternative when lack of solubility of the drug precludes of a solution of any kind. Solubility of drugs has been decreased by the preparation of chemical derivatives or insoluble salts. The derivative is converted into parent drug so neither safety nor efficacy is affected. Oral solutions provide a convenient means of drug administration to neonates and young animals.

2) Tubing products
Oral medication is often administered to horses using a stomach tube. A flexible tube is passed up through the horse nostrils and down into the stomach. An aqueous solution or suspension is desired so that the product can be flushed through the water. Horses are administering certain medications by running a lubricated tube up through the nostrils and down into the stomach. A funnel attached to the tube is held above the horse’s head and liquid medication is poured down the tube. Known as tubing. Normal dose by this method is 10 OZ. Wetting agents are used to increase the flow rate. Thickening and suspending agents are contraindicated to resist the flow.

3) Drenching products
The administration of drug to animals by pouring a liquid medication down an animal’s throat is called “drenching”. The oral administration of cattle, sheep and goats by pouring a liquid product down the animal’s throat is known as drenching. It is performed using either drenching syringe or drenching guns. Thickening agents which promote the thixotropy of the product.

4) Adjuvants
Most solution or suspension contains ingredients other than the active substances to improve the physical or chemical characteristics of the drug and improve acceptability by enhancing odor and taste.

E) Mastitis products
Mastitis has been defined as the inflammation of the mammary gland due to infection by bacteria or mycotic pathogens. It can occur in sheep, goats, cattle and swine. It can result in reduced milk production and it is treated by an systemic administration of antibiotics or an inflammatory infusions.

1) Teat dip
An antiseptic wash or dip before and immediately after milking is used to minimize or prevent access of surface bacteria to the mammary gland.

2) Intramammary infusions
Typical intramammary products or more antibiotics in a petroleum base or mineral oil thickened with polyethylene is used.

E) Pastes and gels
They are defined as any semifluid mass which can be administered from any flexible tube, syringe, package or special dosing devices. Pastes are a popular dosage form for treating cats and horses, and can be easily and safely administered by owners. Semi fluid masses can be administered from a flexible tube, syringe or using a device. The advantage of these are cannot be expelled out animal mouth. Medication may be readily and easily with a paste. A proper consistency to adheres to the tongue or buccal cavity. Three types of vehicles used in the formulation of paste and gels are

a. Aqueous bases
b. Oil or oleaginous bases
c. Organic solvents

Aqueous base is the least expensive vehicle and poses no toxicity. Glycerine, glycols, natural or synthetic gums, polymers used to increase the viscosity, cohesiveness and plasticity. To overcome the separation of water gel, can use absorbing materials like MCC, kaolin, colloidal silicon dioxide, starch. Oleaginous bases consist of vegetable oil with aluminium monostearate, colloidal silica, and xanthan gum. Glycerine, propylene glycol and polyethylene glycol ticket with carboxy vinyl polymers provide organic bases.

Characteristics of pastes
1. When placed in the palm and hand is inverted it should remain without falling
2. When ejected from the applicator, should break cleanly
3. No paste should continue to ooze from the applicator
4. Free from air bubbles

Pellets implants
The subcutaneous implantation of a tablet or pellet will provide a long acting hormone therapy. Pellets implanted on the dorsal surface of a cow’s ear are used for controlling estrous, improving growth and enhancing feed efficiency. Pellet implants of diethylstilbesterol were used in cauponising poultry.

Stability studies of veterinary formulation[6,7]

Introduction
The ultimate user of a veterinary formulation will expect the product to provide the nominal concentration of the drug at any time of administration to the animal except if appropriate qualification appear on the label. To satisfy this criterion an evaluation of product would be required in environmental condition typically expected, but the manufacturer as well as by the distributor, retailer, Veterinarian and final users. A well designed stability study can supply sufficient data for shelf life estimations after only 6 to 9 months of study.

This stability study evaluates the physical and chemical properties of a drug dosage form and determines its ability to resist change.

Testing methods
The U.S. Food and Drug Administration announced in the Federal Register the availability of drug stability guidelines developed by the Bureau of Veterinary Medicine. One of the prior revisions declared that A drug preparation is generally considered unstable when it loses more than 10% of its labelled strength shown as a real loss of stability indicating experiments. Or when it suffers changes of the other various chemical and physical properties. The key to meaningful stability study is the availability of an appropriate analytical procedure. It is seldom necessary for the method to be stability indicating for all structural features of the molecule. The most probable degradation products must be identified and
considered. It may also be in germane, in some cases to discriminate among the intact drug, chemically similar trace impurities and the postulated degradates of these impurities.

A change of dosage form may require different stability indicating analytical procedures for the same drug because different chemical reaction would be expected. This factor is particularly true in veterinary formulation developing because a wide variety of dosage forms of one particular drug are often marketed. Other unique features of these stability studies are that veterinary formulations are subject to an extremely wide variety of environmental conditions. The ranges of temperature, light, humidity etc, to which they can be expected are much less controlled than those for human health formulations. A range of temperature from 0 to 40°c is not uncommon. Incidentally, this range combined with the possibility of extremely high moisture level exposure is a challenge to the packaging engineer of veterinary products as well as a formulator.

Analytical procedures for veterinary drugs which may appear in official compendia can be useless for measuring stability. For instance the official methods of the National Formulary, the animal states pharmacopeia and the Association of Official Analytical chemists for corticosteroids are based on the calorimetric measurements of only one functional group on the C17 side chain. Penicillin is another example demonstrating that official methods are not necessarily stability indicating. Folic acid is an important nutritional supplement administered to poultry. The official USP procedure is based on a nonspecific colorimetric measurements after oxidation of the analyte.

Controlling Authorities of Veterinary Products

Animal Welfare and Animal Husbandry Department, undertaking of the Government of India.
- Animal Health Institute (AHI).
- US FDA (Food & Drug Administration).
- Animal Drugs Availability Act 1996.
- Animal Medicinal Drugs Clarification Act 1968 (AMDOCA)

Specific requirements of regulatory bodies

A) Australia

In contrast with other countries, final approval for marketing of veterinary and agricultural products in Australia is the sovereign right of the individual states, and not the commonwealth government.

However, state approval or registration of veterinary drugs only considered after clearance from the technical committee on veterinary drugs (TCVD), which is on the commonwealth level.

As defined by TCVD a veterinary drug is a preparation intended for use in the mass medication of those farm animals used to produce food for human consumption. This includes such products as dips, sprays, dusts, anthelmintics, medicated stockfeeds and stockfeed additives. It does not include biological products such as vaccines or stockfeed other than medicated feeds or premixes.

Also excluded from clearance by TCVD are products used in horses, dogs, cats and other pets as well as ethical drugs available only on veterinary prescription and intended for use in individual animals.

Under state legislation, veterinary drugs are classified as stock medicines or stockfeeds. Such a product may not be sold in any state unless it is registered with the stock medicines board or similar state authority. This clearance based on safety, toxicology, tissue residue and efficacy data, includes recommendations for poison schedule classification and maximum residue limits (MRL). The TCVD includes one senior officer representing each state and the national health and medical research council (NHMRC), as well as animal secretary from the Australian department of primary industry. Generally the state representative concentrates of the efficacy of the compounds and safety to the target species, nontarget domestic animals, wildlife and the environment.

B) Brazil

In contrast with other countries, Brazil requires registration of both active ingredients and formulated products. Active compounds must be approved before any material can be imported for the purpose of manufacturing finished formulation and the formulated product must then be registered before marketing can commence. Basically, Brazilian regulations require the submission of summarized data in the form of a Technical Report, in Portuguese, duly signed by the responsible technician or other legally qualified technical person of the manufacturing firm. The documents must be legalized and consular certified by the Brazilian consulate in the state or country of manufacture.

In the case of foreign products, the following must accompany the certified reports:

1. Official proof of the competency of the professional who signed the report
2. Official proof that the product is duly licensed and used in the country of origin.

B) European Economic Community (EEC)

Registration in the EEC has grown out of the national requirements of each of its 10 member states: Belgium, Denmark, France, Greece, Holland, Ireland, Italy, Luxembourg, United Kingdom and West Germany. However, EEC approval does not preclude registration at the local level, which must be obtained before a product can be marketed.

The Annex-1 lit. Must be shown for a substance that:

1) It is efficacious.
2) It has no undesirable effect on animal and human health.
3) Its content and nature can be verified in the field.
4) It is not used therapeutically or prophylactically.
5) It is not restricted to use on medical or veterinary prescription for human or animal health.

C) Japan

There are two classifications for product registration in Japan: animal drugs and feed additives. Animal drugs may either require a veterinary prescription or be sold on a nonprescription basis directly to the user. Feed additives are sold only to commercial feed mills for incorporation into finished feeds.

a. Feed additives-

The first law to regulate foodstuffs was promulgated in 1953 Law no 35 to assure feed quality and smooth distribution of finished feed. In 1973, an expert committee was established by the government to study the legislative system to assure safety and quality improvement in animal feed.

Feed additives under the law are defined as those which:

1) Prevent deterioration of feed quality due to fungal growth and other causes.
2) Promote growth of young animals or prevent reduction of productivity due to specific pathogens.
3) Are vitamins and minerals.

b. Animal drugs

The registration of animal drug is the responsibility of the division of animal Drugs of MAFF and is governed by the Pharmaceutical Affairs Law. Included in this law is the animal drug regulations, veterinary antibiotics requirements and powerful and poisonous drug regulations.

Evaluation

1. Products – All tests of a dosage form up to In vitro evaluation
Tiwari et al.  

Int J App Pharm, Vol 6, Issue 1, 20-29

2 Target Animal

Tolerance Studies

1 General tolerance
2 Local tolerance
  • Tolerance testing of Injectables
  • Tolerance testing of products intended for Dermal Applications
  • Tolerance testing of products intended for Oral administration

Bioequivalence Studies

I. Cmax
II. Tmax
III. AUC

CONCLUSION

Animal drug dosage forms have their own requirements & characteristics based on the unique aspects of mammal & avian physiology. Many drugs used in veterinary medicine are not used in human medicine and therefore, pharmacists may not know their attributes. The pharmacist who desires to practice in this area should undertake self-study to learn the chemical, biochemical (metabolism), pharmacological (mechanisms), therapeutic (clinical outcomes), and pharmaceutical (dosage forms) and pharmacokinetic characteristics of these compounds.

REFERENCES