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ADVANCES IN VETERINARY DOSAGE FORMS: AN UPDATED NOTION

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ABSTRACT

Animal provide us with companionship, recreation, and manual labor. Just like a human these animal receive medicine to keep them healthy, and the reasons for producing single dose veterinary dosage forms is the same as those in humans; to permit delivery of an active in a forms that is effective, safe, and able to handled and administered by the end user. This review provides the basic background in the design and evaluation of veterinary dosage forms. The basic dosage forms are describe according to their pharmaceutical characteristic, whereas the description of advanced drug delivery system are organized according to route of administration. In contrast in the veterinary field, the major reasons for developing a drug into a long-acting drug delivery system is to minimize animal handling to reduce the stress to the animals from repeated administration and to reduce the cost of treatment in the terms of money and time spent by the end user on drug administration.

Keywords: Veterinary devices, Quality control tests, Veterinary medication, Boluses

INTRODUCTION

Veterinary dosage forms are drug preparations designed for used in or topical application to, one or more species of domestic animal and/ or other species of veterinary interest. Although the majority of veterinary dosage forms contain the same drug as human dosage forms, some veterinary preparation contain drugs that are not widely used in humans. Examples include benzimidazole anthelmintics, macrolide endectocides, salicylamilide flukicides, and chloramphenicol derivatives [1]. Veterinary pharmacology differs from human pharmacology both in the diversity of species interest and in emphasis placed on the various classes of drug. Some types of dosage forms are suitable for used in humans and certain animal species. They include parenteral solution; conventional tablets and capsules; oral solution and suspensions.

Animal provide us with companionship, recreation, and manual labor [2]. Just like a human these animal receive medicine to keep them healthy, and the reasons for producing single dose veterinary dosage forms is the same as those in humans; to permit delivery of an active in a forms that is effective, safe, and able to handled and administered by the end user. 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 [3].

Veterinary science is vital to study and follow practices to protect animal production practices, herd health and monitoring the spread of disease. We are one of the prominent manufacturers of veterinary formulations like pharmaceutical veterinary formulations, chewable veterinary formulations, protein veterinary formulations, bolus veterinary formulations**,** etc., which are presented in tablet, bolus, powder and liquid [4]. These are widely accepted in both domestic as well as in global regions. Featuring effective curing capability, long shelf life & fast relief, these are prescribed by

veterinary doctors for various ailments in sheep, poultry, cattle, goat and camel**.** Cited below is our entire range of veterinary formulations with their brief descriptions.

Tablets and Boluses:

Solid dosage forms, such as compressed tablets, are one of the most common means of administering medications to humans. These are less popular for animals because administration may be time-consuming, hazardous, and uncertain because one cannot be sure the tablet is swallowed, spit out, or dropped from the mouth after the administrator has left or moved on to another animal. Tablets that are accepted voluntarily by the animal are typically chewed, which exposes the disagreeable taste of some drugs. Thus, the advantage of the dosage form may be lost. This can be overcome in some cases by the use of odors, flavors, or sweeteners [5,6]. Tablets can be coated to differentiate the product by color, to help mitigate offensive-tasting compounds, or to prevent dusting in the bottle. Again, same techniques used for human products are utilized.

Drugs are given on the basis of weight or body surface area, be it for mammals, avian species, or humans. The amount of drug needed for a large mammal, such as a cow, or horse, tends to be stated in mg or g tablet per lb (kg) of body weight. Drugs such as sulfonamides are dosed at relatively high amounts; it is not unusual to prescribe as much as 15 g of drug for each 150 lb of body weight a 750 lb cow or horse would receive 75 g of drug. Various formulations which are available in tablet/bolus forms are manufactured by "Dips VetcareGenevet Pvt. Ltd."Researched and tested formulations such as PETAZOLE-300, LEAV-FIN, PETAZOLE-1500 and many others. LAMISOLE -300 is highly effective and is easily available in the market. It is frequently prescribed against all common round worms of G.I. tract and lung worms in poultry, cattle & sheep. Tablet of LAMISOLE -300 contains **Levamisole Hcl BP 300MG.** Dosage prescribed is 7.5mg Levamisol / kg bwt for elimination of aforesaid infestation in cattle, sheep & goats.

Figure 1: Levamisole Hcl BP 300MG.

A special tablet called a "bolus" is commonly used to provide these large dosages. A bolus is nothing more than a very large tablet, which can range from 3 to 16 g or more. Although commonly called ``horse pills," they are not used exclusively with horses. Because of the difficulty in handling horses, which may be less docile than cows, and the possibility of choking, the bolus form must be used with special care in horses. Boluses are capsule shaped or cylindrical because a round bolus would be unwieldy and difficult to administer or swallow. Boluses are administered by an apparatus called a balling gun, consisting of a barrel with a plunger that can hold one or more boluses. The tube is inserted into the animal's mouth over the base of the tongue, and as the animal swallows the plunger is de-pressed to push the bolus into the gullet. The bolus is thus expelled gently into the gullet, after which it is swallowed by reflex. Stainless steel balling/ bolus gun with plastic head calves, goats and sheep [7].

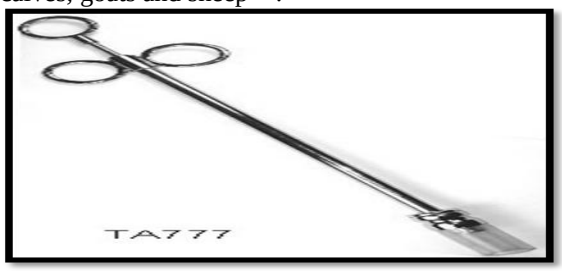

Figure 2: Balling /Bolus Gun

Bolus formulation poses challenges because of the high drug-to-excipient ratio. Less room is left for diluent, binders, and other adjuvants needed to overcome objectionable features of the drug or to facilitate bolus manufacture. In ruminant animals, such as cattleor sheep, it is possible to utilize the concept of long-acting boluses, which stay in the gastrointestinal track for periods of much longer than 12 hours (sometimes days or weeks). This is because solid objects can remain in the ruminoreticular sac, a part of the bovine gastrointestinal tract, indefinitely. The density of the bolus is the critical factor for retention in the sac. The range of density from 1.5 to 8.0 is believed to be desirable for prolonged retention. This is achieved by including excipients such as iron, clay, sodium sulfatedihydrate, and dicalcium sulfate in these formulations Weight and size influence retention, but not as significantly as density. In small animals it is best that oral medications being tested by the animal on its own, thus the special compounding with flavors and in appropriate textures discussed earlier. There are still occasions when an owner may have to open a pet's mouth and administera pill through a ``piller," which is a tube with a plunger [6]. 27g Copper and 500mg

Selenium Bolus for Cows and Cattle. Long acting, Slow Release Intra-ruminal Copper and Selenium Bolus for Routine supplementation of Cows andCattle, Used at 6 month intervals provides a long acting, slow release Copper and Selenium supplementation in bolus form.

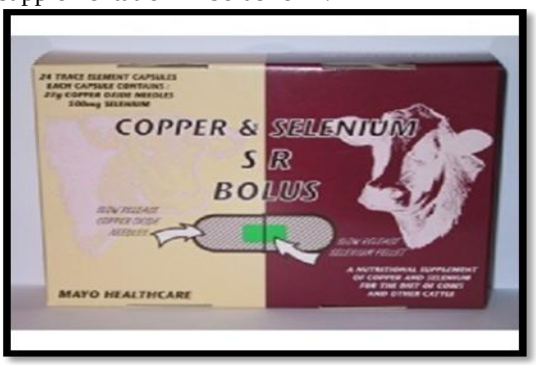

Figure 3: 27g Copper & 500mg Selenium Long Acting, Slow Release, Intra-ruminal Bolus

Capsules:

Capsules are mainly used for dogs and cats, but there are some vitamin and mineral supplement capsules formulated for cattle. There are three main treatment areas using capsules as the dosage form: nutraceuticals, vitamins and minerals, and antimicrobials.

While the typical gelatin capsules used for human can be used for veterinary medicine if the dogs are small (e.g. Sizes no.000, no. 00), there are very large veterinary capsules that range in sizes from no. 13 (2-3g) to no. 7 (14-24g). Interestingly, Capsuline manufacture DOGCaps^{TM} and CATCaps^{TM}, which are capsule containing beef, chicken, or bacon flavoring in the shells to entice dogs and cats to consume the products [3]. RumacinTM cattle capsule is a yeast / microbial supplement fortified with 6 grams of niacin, B vitamins and digestive enzymes for cattle during calving, shipping, and during veterinary treatment. Designed to get the rumen organisms functioning and manage ketosis with research proven levels of niacin.

Figure 4: Microbial, Yeast, Niacin capsules for adult cattle

Feed additives:

Feed additives are preparations used in veterinary medicine to deliver the API(s) via the water or food given to animals. The feed additive may be either a solid or liquid and sometimes is called a premix. Feed additives are further subdivided into three types [8].

TYPE A Medicated Articles

Type A medicated articles are products containing one or more animal APIs, and that are sold to licensed feed mills or producers and are intended to be further diluted by mixing into food or water prior to consumption by the animals. Because these preparations are not actually dosed to animals, they are not considered dosage forms.

TYPE B Medicated Feeds

Type B medicated feeds are products that contain a type A medicated article, or another type B medicated feed, plus a substantial quantity of nutrients (not less than 25% of the total weight). Like type A medicated articles, type B medicated feeds are intended for mixture with food or water and additional nutrients, are not to be fed directly to the animals, and are not considered dosage forms.

TYPE C Medicated Feeds

Type C medicated feeds are made from type A medicated articles or type B medicated feeds and are prepared at concentrations of the API appropriate for administration to animals by mixing in food or water. Administration of type C medicated feeds can be accomplished by blending directly into the feed; top-dressing the preparation onto the animal's normal daily rations; or heating, steaming, and extruding into pellets that are mixed or top-dressed onto the animal's food. Another form of type C medicated feeds is compressed or molded blocks from which animals receive the API or nutrients via licking the block.

- **Preparation**

Type A medicated articles that are liquids are produced by mixing the API(s) with a suitable solvent (e.g., water or propylene glycol). The API(s) is usually dissolved to produce a solution, but suspension products also could be produced. Type A medicated articles that are solids are produced by blending the API with excipients to provide a uniform dosage form when mixed with the animal's feed. Often the API is first mixed with an excipient (e.g., starch or sodium aluminosilicate) that has a similar particle size and can help distribute the API uniformly throughout the final drug product. This pre-blend is then mixed with bulking excipients (e.g., calcium carbonate or soybean hulls). Mineral oil may

be added to aid uniform distribution, to prevent particle segregation during shipping, and to minimize formation of airborne API particles during production of type B or C medicated feeds. Type B or C medicated feeds are produced at licensed feed mills or by farm producers. Type A medicated articles are added to the feeds (e.g., ground corn or oats) during the milling process of making feeds. Liquid type A medicated articles often are sprayed in at set rates, and solid type A medicated articles are added slowly to aid in creating uniform distribution in the feeds. Liquid type A medicated articles can also be mixed in with bulk water sources at prescribed amounts.

- **labeling and packaging**

Type A medicated articles or type B medicated feeds include special labeling to indicate that they should be used in the manufacture of animal feeds or added to the drinking water. The labels indicate that they are not to be fed directly to animals. Also included is a statement indicating ''Not for Human Use''. Type A medicated articles or type B medicated feeds are packaged either in paper bags, often with polyethylene liners, for solids and in plastic containers for liquids. Typical sizes are 50-lb bags or several-gallon containers. Additionally, medicated feed must be stored for several months while they are being used on daily basis to mix the final feeds. Storage can be in hot, moist grain bins or sometimes in the open where the sun and rain can further cause problems.

"Vetbiolyte Supplement", this range of feed supplement contains Sodium chloride, Calcium lactate, Magnesium sulphate, Calcium gluconate, Potassium chloride, Sodium Citrate, Sodium bicarbonate, Ascorbic acid, Dextrose monohydrate and Carriers. Available in packed size of 250 gms, 500 gms and 1 Kg pack size.

1) Provides energy and supportive therapy for chicks immediately after arrival at farm.
2) For energy and supportive therapy during diseases like Nephritis, Nephrosis, Perosis, salmonellosis, Salmonellosis, E. coli and Coccidiosis.
3) In diarrhea and dysentery.
4) To maintain correct osmotic pressure and precise acid-base equilibrium.

Figure 5: Feed Supplements: VETBIOLYTE

Factors that need to be considered in formulating premixes and the choice of carrier are [7]:

1. Drug concentration in the premix.
2. Drug concentration in the final feed: if a drug premix is added to a feed so that the drug level is less than 150 ppm, a carrier is needed to insure adequate dilution.
3. Moisture content of drug and carrier: if the drug is moisture sensitive or the carrier is subject to breakdown or spoilage from moisture levels in the drug or carrier itself, appropriate drying or other steps may be required.
4. Electrostatic charges: fine drug powders will often develop static charges during particle size reduction and flow through material-handling systems. These charges need to be minimized to prevent unmixing or loss in even distribution throughout the premix and subsequent feed.
5. pH extremes: these can frequently be compensated for by use of sodium carbonate to neutralize acid mixtures or calcium phosphate monobasic or fumaric acid to neutralize basic mixtures.
6. Flow: this is important when automatic premix addition equipment is used in modern feed mills. Bridging (an organized structure of product that impedes flow), which inhibits addition of the premix to the feed batch, will cause the mill to shut down until the correct amount of premix is added. This shut-down of the mill can cause considerable consternation to the operators of the mill who are producing multiple batches of feed per day.

The normal standard of premix usage in feed is one part medicated premix to 1999 parts of feed. A properly formulated premix can be used directly in preparing a medicated feed without further dilution. It can be further diluted in the feed mill by the use of in-plant premixes (type B medicated articles), but this would beat the discretion of the feed mill operator. Although the pharmacist may only infrequently have contact with this particular dosage form, there has been a movement to give some feed additive drugs veterinary prescription status, which has been done in several European countries. This may have future implications to those pharmacists practicing in rural areas.

Drinking water medication:

Oral liquids are one of the easier dosage forms to develop. The main challenges are finding a vehicle that result in adequate chemical stability while achieving a solution. The first vehicle choice will be

water. Good understandings of the pH and temperature effect on solubility are needed to ensure no precipitation of the marketed product when exposed to abrupt changes in temperature and pH.

If the water does not solubilize the drug, a cosolvent system is next explored. Vehicles to consider include ethanol, propylene glycol, (low molecular weight), glycerin and triacetin as examples. These can be used alone or in combination to give a truly nonaqueous system. In some cases cosolvents with oleaginous vehicles may be utilized to solubilize the drug [3].

A common form of medicating animals for herd or flock health is through the drinking water. The medications are formulated as:

(a) Dry powders for reconstitution into liquid concentrates to be added to the drinking water or to be added directly to the drinking water or,

(b) Concentrated solutions, which are dispensed directly in drinking water or injected into the drinking water through medication proportioners incorporated into watering lines.

The advantage of medicating through drinking water versus feed is that sick or unhealthy animals will continue to drink water whereas they may not eat. The use of water as the drug medium is limited, however, by the solubility of the drug moiety. Since animals drink twice as much water as they consume feed, the concentration of the drug in the water needs to be only half that of feed. This factor may overcome the problem of limited solubility.

Automatic metering devices or medication proportions are used for treating large numbers of animals. The powder medication is dissolved at the time of administration into water to make a stock solution, which is proportioned into the drinking water system as the water is consumed by the animals. The common dilution in the United States is one fluid ounce of stock solution (or liquid drug concentrate) to 127 ounces of water, producing a one fluid ounce per gallon dilution. Whether a product is formulated as a dry powder, dispensing tablet, or liquid concentrate, the product development/ compounding pharmacist must be concerned with the effects of the properties of the diluting water media. Tablet or granule hardness, buffer capacity, pH, and total dissolved solids all play a role in the solubility rate and availability of the drug substance, as well as its stability [7].

In addition, dry products are usually formulated with a sugar diluent such as lactose or dextrose. The use of these may cause a build-up of bacteria and fungi in water lines when the sugar level is high for an extended period of time. In the product development laboratory, medicated drinking water samples must be prepared from these formulations using a range of hard and soft waters and stored at 25^{o}C and 37±40^{o} C in metal containers or troughs (galvanized iron or rusty metal) to simulate the worst possible conditions of use. The drug stability in the drinking water should be adequate for the storage length of time listed on the label. Consideration also has to be given when formulating a liquid concentrate using solvents other than water of the possibility of precipitation or recrystalization of the drug when diluted with water. All of the above factors make products an interesting and challenging task.

Parenteral dosage forms:

Parenteral dosage forms and delivery systems include injectables (i.e., solutions, suspensions, emulsions, and dry powders for reconstitution), intra-mammary infusions, intra-vaginal delisystems, and implants [9].

A **solution** for injection is a mixture of two or more components that form a single phase that is homogeneous down to the molecular level. "Water for injection" is the most widely used solvent for parenteral formulations.

A **suspension** for injection consists of insoluble solid particles dispersed in a liquid medium, with the solid particles accounting for 0.5-30% of the suspension. The vehicle may be aqueous, oil, or both. Injectable suspensions are commonly used.

An **emulsion** for injection is a heterogeneous dispersion of one immiscible liquid in another; it relies on an emulsifying agent for stability. Parenteral emulsions are rare because it is seldom necessary to achieve an emulsion for drug administration.

A **dry powder** for parenteral administration is reconstituted as a solution or as a suspension immediately prior to injection. The principal advantage of this dosage form is that it overcomes the problem of instability in solution

Mastitis **intra-mammary infusion products** are available for lactating and non-lactating (dry) cows. Lactating cow intra-mammary infusions should demonstrate fast and even distribution of the drug and a low degree of binding to udder tissue. These properties result in lower concentrations of drug residues in the milk [10,11].

Intra-vaginal delivery systems include controlled internal drug release (CIDR) devices, progesterone-releasing intra-vaginal devices (PRID), and vaginal sponges. These systems are used for oestrus synchronization in sheep, goats, and cattle

The majorities of implants used in veterinary medicines are compressed tablets or dispersed matrix systems in which the drug is uniformly dispersed within a non-degradable polymer.

Oral pastes and gels:

Pastes and gels are semi-fluid masses that can be administered from a flexible tube, syringe, package, or other specialized dosing device. The advantage of

a paste or gel dosage form is that it cannot be expelled from the animal's mouth as readily as a tablet or liquid. Also, mass medicating of animals can be achieved rapidly and easily with a paste medication using a multiple-dose dispenser such as a syringe. A paste of the proper consistency adheres to the tongue or buccal cavity and is not readily dislodged. The animal will eventually end up swallowing it. Characteristics of a suitable paste formulation are [7]:

1. When placed in the palm of the hand and the hand is inverted (palm down), it should remain there without falling.
2. When the paste is ejected from the applicator, it should break free cleanly when rubbed against a flat surface.
3. No paste should continue to ooze from the applicator after the dose has been ejected.
4. The paste or gel should be free from air bubbles or voids.
5. Only a minimum of force should be needed to expel the paste from the dispensing device.

Biotene Maintenance Gel is pet toothpaste that provides long-lasting protection to your pet's teeth and gums. The plaque-removing gel contains Bio-Active Enzymes that effectively inhibit odor-causing bacteria. These 6 enzymes (Lysozyme, Lactoferrin, Glucose Oxidase, Lactoperoxidase, Mutanase and Dextranase) each have their own unique properties, but the combination provides a powerful antimicrobial defense system against plaque and bacteria. Not only that, but it also relieves, soothes and protects their mouth tissues against dryness, irritation, inflammation and redness. The gentle formulation has a pleasant flavor and is safe for pets of all ages. Contain no Xylitol, alcohol, chlorhexidine or chlorine compounds, making it a safe part of your pet's daily oral care program.

Figure 7: Biotene veterinarian oral care kit and maintenance oral gel.

The three types of vehicles used in formulating a paste or gel are aqueous bases, oil or oleaginous bases, and organic solvents.

An aqueous base is the least expensive vehicle and poses no toxicity problems. A solution of the drug in water or water and cosolvent is made. Glycerin, glycols, natural and synthetic gums, and or polymers are used to increase viscosity, cohesiveness, and plasticity. To overcome syneresis, or water separation in the gel, a common problem with aqueous bases, one can use absorbing materials such as microcrystalline cellulose, kaolin, colloidal silicon dioxide, starch, etc.

Oleaginous bases consist of vegetable oil thickened with agents such as aluminum monostearate, colloidal silica, and xanthan gums. The lubricant properties of the oil make these formulations less adhesive than water bases.

Glycerin, propylene glycol, and polyethylene glycol thickened with carboxy vinyl polymers (CarboxamerNF) provide organic solvent bases. Consistencies ranging from soft jelly to peanut butter can be achieved.

A paste is administered to an animal volumetrically. The drug level and density of the paste must be known to determine the amount of drug delivered per given volume. This takes trial and error in the formulation process to arrive at the volume of paste necessary to provide the required dose. Sometimes pastes are used in small animals by applying them to an animal's fur on the front paws. The animal will lick the paste off to stay clean.

Drenches and tubing products:

Horses are administered 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 the liquid medication is poured down the tube. This is known as ``tubing."

The normal dose for a horse by this method is approximately 10 fluid ounces. It needs to be formulated so that the amount will flow through the tubing (i.e., 6 1/2 ft × 3/8 in.) in 60 seconds. Wetting agents are used to increase flow rate. Thickening or suspending agents are contraindicated since the formulations will thicken and resist flow when shear is removed.

The administration of a drug to animals by pouring a liquid medication down an animal's throat is called ``drenching." Drenches are dispensed via syringe or drenching guns. The viscosity should be adequate to prevent dripping from the syringe during movement from the drug container to the animal. Drenching gun can utilize formulations that are less viscous since leakage from the gun is not a major problem. Too

viscous a product may cause administrator fatigue when large numbers of animals are dosed. These drenches and tubing products are often given over extreme ranges of temperatures in field conditions. The formulator must take this into consideration when developing the dosage formula and testing it in the administration equipment.

Topical dosage forms:

The topical dosage forms available for treating animals include solids (dusting powders), semisolids (creams, ointments, and pastes), and liquids (solutions, suspension concentrates, suspoemulsion, and emulsifiable concentrates). Of special interest are transdermal delivery systems that elicit clinical responses by carrying medications across the skin barrier to the bloodstream. Examples of these are transdermal gels and patches that are used in companion animals [12].

A **transdermal delivery gel** consists of a vehicle, most commonly pluronic lecithin organogel (PLO gel), which delivers drug via the transdermal route to the bloodstream. The micellar composition of PLO gel enhances skin penetration of the pharmaceutical agent present in the formulation. PLO gel is generally well tolerated and is nontoxic if ingested. However, not all drugs are suitable for transdermal application and there are relatively few studies of the bioavailability of drugs from compounded transdermal gels. Transdermal gels are used to deliver drugs to treat several diseases in dogs and cats, including undesirable behavior, cardiac disease, and hyperthyroidism. The dose is applied to the inner surface of the pinnae, thereby offering ease of administration, especially in cats.

A **transdermal delivery patch** typically consists of a drug incorporated into a reservoir, a protective backing layer, a rate-limiting release membrane, and an adhesive layer for securing the patch to the skin. The physicochemical properties of a drug suitable for transdermal delivery ideally include low molecular weight (<500 daltons), high potency, water solubility (to facilitate movement of the drug out of the reservoir and to allow passage through the epidermal and dermal layers of the skin), and lipid solubility (to permit penetration of the stratum corneum of the skin). Fentanyl, a synthetic opioid agonist, is delivered by transdermal patch in dogs, cats, and horses.

There are several unique topical dosage forms for animals. Four types of which the pharmacist should have a basic understanding or awareness are: (a) pour- on/spot-on applications, (b) dust bags, (c) dips, and (d) flea and tick collars [5]. These are used for treatment and prevention of internal and external parasites. The control of internal and external parasites of companion and food-producing animals has led to the development of specialized dosage forms, delivery systems, and application methods that are unique to veterinary medicine.

- **Pour-On/Spot-On Applications:**

These liquid products affect systemic activity after being poured onto an animal's backline or applied as a one-spot concentrate on the animals back or rump. Some spot-on products now help small animals combat fleas and ticks. These products are generally preferred to flea and tick collars. The oils from the drug mix with the pet's natural oils. They act as a neurotoxin against the ectoparasites. In cattle, spot-ons are mainly used for control of grubs and lice. However, there is one pour-on/ spot-on product (levamisole) that has broad-spectrum anthelmintic activity. These formulations contain organophosphorus insecticides or the anthelmintic dissolved in organic solvents, such as dimethylsulfoxide and/ or aromatic hydrocarbons. The advantages of these formulations are:

1. Risk of trauma and inhalation pneumonia associated with drenching or damage at injection site (for parenteral products) are eliminated.
2. No special skills are required for application since they are administered topically by use of sprays or spotter bottle (a bottle with a squeeze- on applicator).
3. Sterile precautions are not necessary.
4. Troublesome animals are dosed easily with safety to the person performing the application.
5. Speed of treatment is quick.

- Dust Bags:

Cattle are treated with insecticide powders through use of a device called a dust bag. Dosing is accomplished by the animals brushing against the bag as they walk beside or under it. The bag has an inner porous storage bag containing the insecticide dust formulation. This is protected from the elements by an outer protective waterproof skirt open to the porous dust bag at the bottom.

The cattle can have free-choice application or are forced to use dust bags depending upon where they are hung. Forced-use bags are hung in doorways, lanes, gateways, etc. Free-choice applications can be achieved by suspending the bags from overhead structures, like a tree or pole. One would be surprised at the will ingness of the majority of range cattle to come to a free-choice application sit

- Dips:

For control of ectoparasites in economic animals, dipping is an extensively used method of sheep and cattle for external parasites requires a dipping vat,

which may be a portable unit or a permanent in-ground structure shielded from direct sunlight by roofing. A draining pen located at the exit of the vat allows dip wash draining off treated animals to return to the vat. Dip chemicals are usually formulated as aqueous solutions, emulsifiable concentrates, or suspension concentrates, all of which are diluted with water prior to use. The high costs associated with plunge dipping relate principally to the costs of chemicals for charging large vats, labor, and the disposal of the hazardous wastes. A dip formulation containing the drug is diluted in a large dipping bath through which the animal is driven. This bath must be long, wide, and deep enough to cause immersion of the animal. The formulation of the ectoparasiticide is challenging. It must not be inactivated by matter that accumulates in the dipping bath and should maintain stability throughout a range of concentrations and temperatures. In addition, it must be nontoxic to the animal but toxic to the ectoparasites. This dosage form is used in both large and small animals.

Plunge dips must be managed properly, and the pesticide maintained at the concentration recommended by the manufacturer. Dipping of sheep and cattle is associated with "stripping" of the active ingredient from the dip wash, e.g., pesticide loss from the dip wash occurring at a greater rate than water loss, and is categorized as mechanical or chemical. In the case of sheep, mechanical stripping results from the fleece acting as a sieve toward the active ingredient, with the degree of filtration being primarily determined by particle size. Chemical stripping is due to the preferential absorption of pesticide by the fleece. To counteract stripping, a complex dip management regimen that involves reinforcement and ''topping-up" is used. Reinforcement refers to the addition of undiluted chemical product to the dip without the addition of water, whereas topping-up refers to the addition of water and undiluted chemical product to the dip vat to return the volume to the starting level. Proper dip management also minimizes the contamination of the dip with organic matter. This requires that the race leading to the vat is constructed of concrete or slats to remove dirt from the animals' feet and for animals to be held in a yard overnight prior to dipping, during which time they are offered water but no food.

Shower dips are less labor intensive than plunge dips and are cheaper to operate. A typical shower dip consists of a sump containing the dip wash, a pump, and a showering pen constructed with a concrete floor and fitted with an overhead rotating boom with nozzles and fixed nozzles near ground level. There are two types of shower dips: a conventional shower dip in which the sump volume is periodically maintained by adding fresh dip wash, and a constant replenishment shower dip in which a small-volume sump is continuously filled from a large-volume supply tank to maintain dip levels. Proper dip management requires attention to the factors described above for plunge dipping [13]. In addition, all equipment must be functioning properly for the fleece to become saturated. Sheep should not be dipped (by either the plunge or shower method) until shearing wounds have healed to avoid clostridial infections or caseous lymphadenitis caused by *Corynebacterium pseudotuberculosis*. Moreover, the correct use of bacteriostats is recommended to prevent post-dipping lameness caused by *Erysipelothrix insidiosa*.

- Flea and Tick Collars:

This dosage form will be most familiar to the pharmacist since it is used for companion animals (dogs and cats) and is sold in most drugstores, supermarkets, and animal health product centers. There are two types of flea and tick collars, also known as slow-release pesticide generators: vaporous and powder-producing collars. Both contain the insecticide and a plasticized solid thermoplastic resin. The vaporous collar contains a relatively high- vapor-pressure liquid pesticide mixed throughout the collar. The pesticide is slowly released and fills the atmosphere adjacent to the animal's surface with a vapor of pesticide that kills the pest but is 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 or molecules of the pesticide migrate from within the body of the resin and form a coating of particles, known as ``bloom," resembling a dust or powder on the collar surface.

Ticks and fleas tend to concentrate in or migrate through the neck area of the animal. As they do this, they contact the active pesticide on or released by the collar and are killed. Powder-producing collars have an advantage over vaporous ones in that by the movement of the dog or cat, the powder crystals (bloom) are rubbed or wiped onto the fur, which expands the contact area allowing it to continue to control the ticks and fleas.

PRODUCT QUALITY AND EFFICACY:

Before they can be put on the market, the efficacy of veterinary products is confirmed by trials under field conditions [14].

- **High Standards of Purity and Consistency**

Pharmaceutical quality is an essential ingredient of product safety, and requires the product to be manufactured according to specific standards of purity and consistency. These standards apply throughout the production and formulation process.

Stability studies ensure that the product retains its potency, efficacy and safety, for the full duration of the shelf-life.

- **Testing Methods are continuously being improved**

The pharmaceutical manufacturer is required to guarantee that a medicine contains only those ingredients that are specified in the data file - nothing more, nothing less - and in exactly the proportions indicated. Analytical test methods used to achieve this are continuously being improved.

The animal health industry has, on own initiative, introduced sterility tests and visual inspection of random samples as additional control measures. As an example of the efforts made to guarantee consistent product quality, water used for dissolving the active substance of a medicine is distilled twice, sterilized and then kept at 85°C until used.

- **The Product will Live Up to its Claims**

Data must also be provided to prove that the product meets a specified level of efficacy in treating or preventing a particular medical condition. Thus the customer can be assured that, when used as directed (correct dose-rate, frequency and duration of treatment), a product will meet its label claims. To support this claim, a product is tested extensively in the laboratory, in disease challenge studies and finally in field trials, which must demonstrate that it works under conditions of practical field use.

- **The Leaflet is Part of the Product**

An animal health product does not consist of the medicine alone. The product name together with its label and leaflet (giving indications, contra-indications, warnings and withdrawal periods) are also essential parts of the product and its registration process. The registration authorities must also approve these and any changes to them.

Dosage Forms of Active Pharmaceutical Ingredients apply to all veterinary dosage forms or preparations of the type defined, however, a valid interpretation of the appropriateness of a test or requirement for compliance with the test given under each dosage form [15].

1. Dip Concentrates

Dip concentrates are preparations for the prevention and treatment of ectoparasitic infestations of animals. They contain one or more medicaments, usually in the form of wettable powders, pastes or solutions from which diluted suspensions or emulsions are prepared by appropriate dilution with the recommended liquid. The diluted preparations are applied by complete immersion of the animal or by spraying, as appropriate. They contain suitable antimicrobial preservatives.

Labeling: The label states (1) the name(s) and proportion(s) of medicament(s); (2) the name and proportion of any added antimicrobial preservative; (3) the name and quantity of the diluent and the manner of preparing the diluted dip solution or spray; (4) any special precautions to be taken for use of the preparation; (5) the storage conditions; (6) the date after which the preparation is not intended to be used. If the preparation contains an organophosphorus compound the label also states (1) that the preparation contains an organophosphorus compound; (2) and special precautions on the use of the preparation.

2. Premixes

Premixes are mixtures of one or more active ingredients with suitable bases intended for mixing with feedstuffs before administration to the animals. They are used to dilute medicament(s) with the feed and are usually issued as pellets, granules or powders. If issued as granules, these are free flowing and free from aggregates. Suitable precautions are taken during manufacture for ensuring that the premix is homogeneous.

Unless otherwise stated in the individual monograph, the concentration of the premix in medicated feedstuffs is not less than 0.5%.

Tests:

Loss on drying: Not more than 15.0 per cent, determined on 3 g by drying in an oven at 105º for 2 hours.

Labeling: The label states (1) the strength in terms of the amount of active ingredient(s) as a percentage; (2) the category of animal for which the premix is intended to be used; (3) the directions for the preparation of the medicated feed; (4) where applicable, the minimum interval between the stoppage of feeding of the diluted premix and the slaughter of the animal for human consumption; (5) any special precautions to be taken for use of the premix; (6) the storage conditions; (7) the date after which the preparation is not intended to be used.

3. Veterinary Oral Liquids

Veterinary oral liquids intended for administration in large animals may also be called Drenches.

4. Veterinary Oral Powders

Veterinary Oral Powders are intended for oral administration, usually after dilution in drinking water or the feed. They may be in the form of soluble or wettable powders.

Labeling: The label states that (1) for single dose containers, the name and quantity of active medicament(s) per container; (2) for multiple dose

containers, the name and quantity of active medicament(s) by weight; (3) the name of any added antimicrobial preservative(s); (4) the directions for use of the preparation.

5. Intramammary Infusions

Intramammary Infusions for Veterinary Use; Intramammary Injections. Intramammary Infusions are sterile products intended for injection into the mammary gland through the teat canal. They are solutions, emulsions or suspensions or semi-solid preparations containing one or more active ingredients in a suitable vehicle. They may contain stabilizing, emulsifying, suspending and thickening agents. If sediment is formed in a suspension, it is readily dispersible on shaking. In emulsions, phase separation may occur but this is readily miscible on shaking. There are two main types of Intramammary Infusions. One is intended for administration to lactating animals as qualified by the term Lactating Cow/Buffalo and the other, qualified as Non-lactating or Dry Cow/Buffalo, is intended for administration to animals at the end of lactation or during the non-lactating period for the prevention or treatment of infection during the dry period. Intramammary Infusions are prepared by dissolving or suspending the sterile medicaments in the sterilized vehicle using aseptic precautions, unless a process of terminal sterilization is employed.

Container: Intramammary Infusions are usually supplied in single dose containers for administration into a single teat canal of an animal. If supplied in multiple dose containers, aqueous preparations contain an antimicrobial preservative in adequate concentration except when the preparation itself has antimicrobial properties. The containers are made as far as possible from materials that meet the requirements for Parenteral Preparations intended for use in human beings. The containers are sealed so as to exclude micro-organisms and each container is fitted with a smooth, tapered nozzle to facilitate the introduction of the infusion into the teat canal. The containers are sterilized and filled aseptically unless the preparation is subjected to a process of terminal sterilization.

Tests

Sterility: Intramammary Infusions comply with the test for sterility, using Method A or B, as appropriate, using the contents of 10 containers mixed thoroughly before use in the test. Use for each medium 0.5 to 1.0 g or 0.5 to 1.0 ml, as appropriate, of the mixed sample.

Storage: Store in sterile, single dose or multiple doses, tamper evident containers.

Labeling: The label states (1) the strength in terms of the weight or the number of Units of activity of the active ingredient(s) or that may be expressed from the container using normal techniques; (2) whether the preparation is intended for use in lactating cow/buffalo or in dry or non-lactating cow/buffalo; (3) for Intramammary Infusions (Non-lactating or Dry Cow/Buffalo), that the preparation is not intended for use in lactating animals; (4) in the case of infusions in multiple dose containers, the name of any added antimicrobial preservative.

6. Veterinary Parenteral Preparations

Veterinary Parenteral Preparations prepared with oily vehicles are not meant for intravenous administration but are suitable for intramuscular or subcutaneous use. Veterinary Parenteral Preparations comply with the appropriate requirements for Parenteral Preparations (Injections) that are given in the chapter on General Monographs on Dosage Forms of Active Pharmaceutical Ingredients.

7. Veterinary Tablets

Veterinary tablets are usually solid, circular cylinders the end surfaces of which are flat or biconvex and the edges of which are bevelled except that those weighing 5 g of more may be elongated or biconical.

Tests

Disintegration: The test may have to be suitably modified in the case of large tablets; the discs may have to be omitted because they would otherwise be dislodged from the disintegration tubes. It may also be necessary to adjust the volume of the disintegration medium so that the tablet does not break the surface of the medium at the top of the upstroke, care being taken to apply the minimum practical volume of liquid for this purpose. For certain tablets where the diameter of the tablet may not permit adequate movement of the disintegration medium, the apparatus and the method should be suitably modified.

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 [16]

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 and secretory 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.

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.

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.

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.

- 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.

- 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.

CONCLUSION

Veterinary pharmaceuticals serve an important role in preserving and restoring animal health, thereby also enhancing human wellbeing. Efficient development of safe and effective new animal drug continued availability of approved products is essential to maintenance of animal health and productivity. For

animal companions, veterinary pharmaceuticals are used to treat a range of disease condition similar to those of human patients. 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.

CONFLICT OF INTEREST: Author declares no conflict of interest.

Table 1: Marketed oral controlled release pharmaceuticals product:

Brand Name	Active Ingredient(s)	Therapeutic Segment	Pack Details	Animal Species
Zenvet Bolus	Closantel 1000mg	Ectoendecto Paraticide	4 Bolus in a blister	Cattle / Buffalo / Camel / Horse
Fentas Bolus	Fenbendazole 1.5gm/3gm	Endoparasiticide	1.5 gm - 4 Bolus in a blister/3 gm- 1 Bolus in a blister	Cattle / Buffalo / Camel / Horse
Ecotas	Sacchromysescerevisiae +Lactobacillus sporogenes+ Aspergillusoryzae	Fortified Synbiotic Combination	8 Bolus in a blister	Cattle / Buffalo / Sheep / Goat / Camel
Eazypet	Praziquantel 50mg +pyrantelpamoate 144mg + fenbendazole 500mg	Endoparasiticide	2 Tablets in a blister/10 Tablets in a blister	Dog / Cat

Table 2: Marketed oral controlled release pharmaceuticals product:

Brand Name	Active Ingredient(s)	Therapeutic Segment	Pack Details	Animal Species
Alzonic	Albendazole 3% w/v + Niclosamide 10% w/v	Endoparasiticide	500 ml and 1000 ml bottles	Sheep / Goat
Zenvet Solution	Closantel 15% w/v	Ectoendectoparaticide	30ml, 100ml and 500ml bottles	Cattle / Buffalo / Sheep / Goat / Camel / Pig / Horse
Feed-O-Tas	Oranic Acids with silica and bentonite	Feed Acidifier	Poultry	1 kg and 25 kg bags
Fentas Powder	Fenbendazole 25% w/w	Endoparasiticide	Cattle / Buffalo / Sheep / Goat / Dog / Camel / Horse	60 gm and 120 gm pack
E-Booster	Gluconeogenic precursor + Nicotinamide + Cyanocobalamin	Energy booster	Cattle / Buffalo	1 liter

Table 3: Marketed parenteral controlled release pharmaceuticals product:

Brand Name	Active Ingredient(s)	Therapeutic Segment	Pack Details	Animal Species
AC-Vet	Ampicillin 1 gm + Cloxacillin 1 gm	Anti-Infective	2 gm vial with WFI	Cattle / Buffalo
AC-Vet Forte	Ampicillin 1.5 gm + Cloxacillin 1.5 gm	Anti-Infective	2 gm vial with WFI	Cattle / Buffalo
Zubion	Buparvaquone 50 mg	Anti Protozoal	2ml and 20 ml vials	Cattle / Buffalo / Camel / Horse
Anistamin	Chlorpheniramine maleate 10 mg/ml	Anti-Histaminic	50ml and 100 ml vials	Cattle / Buffalo / Sheep / Goat / Dog / Cat / Camel / Horse / Pig

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