Routes of Administration and Dosage Forms

A diverse range of dosage forms and delivery systems has been developed to provide for the care and welfare of animals. The development of dosage forms draws on the discipline of biopharmaceutics, which integrates an understanding of formulations, dissolution, stability, and controlled release (pharmaceutics); absorption, distribution, metabolism, and excretion (pharmacokinetics, PK); concentration-effect relationships and drug-receptor interactions (pharmacodynamics, PD); and treatment of the disease state (therapeutics). Formulation of a dosage form typically involves combining an active ingredient and one or more excipients; the resultant dosage form determines the route of administration and the clinical efficacy and safety of the drug. Optimization of drug doses is also critical to achieving clinical efficacy and safety. Increasingly, a PK/PD model that describes the drug response is the basis of dose optimization. The PK and PD phases are linked by the premise that free drug in the systemic circulation is in equilibrium with the receptors. The PD phase generally involves interaction of the drug with a

drug effect (see Drug Concentration and Effect).

Drug delivery strategies for veterinary formulations are complicated by the diversity of species and breeds treated, the wide range in body sizes, different husbandry practices, seasonal variations, cost constraints associated with the value of the animal being treated, the persistence of residues in food and fiber (see Chemical Residues in Food and Fiber), and the level of convenience, among other factors. Innovative solutions have been developed to meet many of these challenges (eg, the convenient dosing option offered by topical spot-on formulations to treat external and internal parasites on dogs and cats, the microencapsulation of NSAIDs as a way to mask taste when these agents are added to the rations of horses). The anatomy of the GI tract of ruminants presents unique opportunities for controlled-release drug delivery systems, and many such systems are on the market. For example, controlled-release boluses have been developed to deliver antimicrobials, anthelmintics, production enhancers, nutritional supplements, and other drugs.

ORAL ROUTE OF ADMINISTRATION AND DOSAGE FORMS

The oral route of administration is frequently used in both companion and food animals. In dogs and cats, tablets, capsules, solutions, and suspensions are administered orally; pastes are also applied to the forelimbs of cats from which they are licked and ingested. In horses, solutions and suspensions are administered by nasogastric tubes, pastes are applied to the tongue, and granules are added to rations for ingestion. The oral route of administration is the most widely used in cattle, pigs, and poultry. Formulations range from premixes and drinking water additives to licks, pastes, drenches, tablets, capsules

and boluses. Oral dosage forms are usually intended for systemic effects resulting from drug absorption from the GI tract; however, some oral suspensions, eg, kaolin, are intended to produce local effects, and these are not absorbed. Disadvantages of the oral route of administration include the relatively slow onset of action, the possibilities of irregular absorption, the destruction of acid-labile drugs in the stomach, and the unsuitability of this route for many high-molecular-weight drugs. Oral dosage forms require careful pharmaceutical formulation.

Oral dosage forms comprise liquids (solutions, suspensions, emulsions, elixirs, and syrups), semisolids (pastes), and solids (tablets, capsules, powders, granules, premixes, and medicated blocks). These dosage forms together with examples of modified-release delivery systems for ruminants are discussed below.

A **solution** is a mixture of two or more components that form a single phase that is homogeneous down to the molecular level. Solutions offer several advantages over other dosage forms. Compared with solid dosage forms, solutions are absorbed faster and generally cause less irritation of the GI mucosa. Moreover, phase separation on storage is not a concern with solutions, as it may be for suspensions and emulsions. The disadvantages of solutions include susceptibility to microbial contamination and the hydrolysis in aqueous solution of susceptible active ingredients. In addition, the taste of some drugs is more unpleasant when in solution. A range of additives is used in the formulation of oral solutions, including buffers, flavors, antioxidants, and preservatives. Oral solutions provide a convenient means of drug administration to neonates and young animals

A **suspension** is a coarse dispersion of insoluble drug particles, generally with a diameter >1 µm, in a liquid (usually aqueous) medium. Suspensions are useful to administer insoluble or poorly soluble drugs or when the presence of a finely divided form of the material in the GI tract is required. An example of the latter is the treatment of “frothy bloat” with dimethyl polysiloxanes, which relies on a dispersion of finely divided silica in the forestomach of ruminants. The taste of most drugs is less noticeable in suspension than in solution, because the drug is less soluble in suspension. Particle size is an important determinant of the dissolution rate and bioavailability of drugs in suspension. In addition to the excipients described above for solutions, suspensions include surfactants and thickening agents. Surfactants wet the solid particles, thereby ensuring the particles disperse readily throughout the liquid. Thickening agents reduce the rate at which particles settle to the bottom of the container. Some settling is acceptable, provided the sediment can be readily dispersed when the container is shaken. Redispersion of the suspension may not be achievable if the sediment has packed closely to form a hard mass, a process known as "caking."

An **emulsion** is a system consisting of two immiscible liquid phases, one of which is dispersed throughout the other in the form of fine droplets; droplet diameter generally ranges from 0.1–100 µm. The two phases of an emulsion are known as the dispersed phase and the continuous phase. Emulsions are inherently unstable and are stabilized through the use of an emulsifying agent, which prevents coalescence of the dispersed droplets. Creaming, as occurs with milk, also occurs with pharmaceutical emulsions. However, it is not a serious problem because a uniform dispersion returns upon shaking.

increased likelihood of the droplets coalescing and the emulsion "breaking." Other additives include buffers, antioxidants, and preservatives. Emulsions for oral administration are usually oil (the active ingredient) in water, and they facilitate the administration of oily substances such as castor oil or liquid paraffin in a more palatable form.

An **elixir** is a sweetened, usually hydroalcoholic solution of a bitter or nauseous drug intended for oral administration. The hydroalcoholic character of elixirs allows, within limits, both water-soluble and alcohol-soluble medicinal substances to be maintained in solution. The proportion of alcohol in elixirs varies widely, a characteristic used to advantage to solubilize medicinal agents. If the active ingredient is sensitive to moisture, it may be formulated as a flavored powder or granulation and reconstituted in water immediately before oral administration. Nonmedicated elixirs are used as the vehicles for pharmaceutical formulations.

A **syrup** is a concentrated aqueous solution of sugar or a sugar substitute with or without flavoring agents and a water-soluble drug. Sucrose is the most frequently used sugar, and syrups usually contain 60%–80%. Syrups may also contain cosolvents, solubilizing agents, thickeners, or stabilizers. Nonmedicated syrups are used as vehicles for water-soluble drugs.

A **paste** is a two-component semisolid in which drug is dispersed as a powder in an aqueous or fatty base. The particle size of the active ingredient in pastes can be as large as 100 µm. The vehicle containing the drug may be water; a polyhydroxy liquid such as glycerin

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