BASICS OF VETERINARY COMPOUNDING
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OBJECTIVES
• Review veterinary pharmacology
• List compounding Guidelines (USP 795)
• Choose appropriate equipment and supplies required to compound veterinary preparations
• Describe different formulations
• Choose appropriate flavors for palatability
• Perform calculations necessary to compound veterinary preparations

UNITED STATES PHARMACOPEIA (USP)
• Public health organization that sets the standards for identity, strength, quality, and purity of consumable products.
  • Medication
  • Food ingredients
  • Dietary supplements
• Not a regulatory agency
• USP provides:
  • Official drug monographs
  • Uniform formulations
  • Stability studies
  • Documented Beyond Use Dates (BUD)

USP 795 DEFINITION
• The preparation, mixing, assembling, altering, packaging, and labeling of a drug, drug-delivery device, or device in accordance with a licensed practitioner’s, medication order, or initiative based on the practitioner/patient/pharmacist/compounder relationship in the course of professional practice.
• Compounding includes
  • Preparation of drug dosage forms for both human animal patients
  • Preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns
  • Reconstitution or manipulation of commercial products that may require the addition of one or more ingredients
  • Preparation of drugs or devices for the purposes of or as an incident to, research (clinical or academic), teaching, or chemical analysis
  • Preparation of drugs and devices for prescriber’s office use where permitted by federal and state law

COMPOUNDING
• Historically, veterinarians have prepared concoctions, mixtures, and remedies for their patients because there were few approved formulations on the market for animals.
• Now, there are more available drugs for animals, and pharmaceutical science has provided for a better understanding of the factors contributing to poor drug bioavailability, instability, and physical incompatibility.
• Over the last several years, questions concerning the practice of compounding have been raised, particularly with respect to stability, purity, and strength when the original dosage form of the drug is altered.

COMPOUNDING
• A prescription written by a veterinarian generally includes the animal species and/or pet’s name and the name of the owner. A written prescription may be presented at the pharmacy by the patient or caregiver, or it may be transmitted from the prescriber by telephone or by other electronic means
BEYOND USE DATES USP 795

- The date after which a compounded nonsterile preparation should not be used
  - Nonaqueous Formulations: no longer than 6 months or the earliest expiration date of any ingredient used, whichever is shorter, and stored at controlled room temperatures.
  - Water Containing Oral Formulations: no longer than 14 days or the earliest expiration date of any ingredient used, whichever is shorter, and stored at controlled cold temperatures. This includes water being added as an ingredient or water as a component of any ingredient used.
  - Water Containing Topical/Dermal and Mucosal Liquid and Semisolid Formulations: no longer than 30 days or the earliest expiration date of any ingredient used, whichever is shorter, and stored at controlled room temperatures. This includes water being added as an ingredient or water as a component of any ingredient used.
- If a pharmacist feels that a BUD for a particular product is inadequate, they may use professional judgment to assign a different BUD.
- The pharmacist should be prepared to defend that judgment.

FORMULATION GUIDELINES

- If available, use manufactured products
- When manufactured products are not available
  - Find recipes specific to species
  - Find general recipes specific to animals in general
  - Research literature on excipients.
- Some excipients can be fatal to animals.

FORMULATION GUIDELINES

MEDICATIONS FATAL TO ANIMALS

- While an (NSAID), like aspirin, ibuprofen, and naproxen, is safe and effective in people, the drug may not be safe and effective in dogs because the drug may:
  - Last longer
  - Have a higher absorption rate in the stomach and small intestine; and
  - Reach higher blood levels.
- These differences may lead to toxic effects in dogs, such as stomach problems as well as liver and kidney damage.
- Cats are more sensitive than dogs to the side effects of NSAIDs because they aren't able to break down the drugs as well.
- Acetaminophen is NOT an NSAID but it is fatal to cats.
- Hepatotoxicity (dogs) and red blood cell oxidative injury in cats

OTHER POTENTIALLY FATAL MEDICATIONS/FOOD

- Benzocaine given to cats can cause Red blood cell oxidative injury, hemolytic anemia
- Chamomile given to cats causes emesis, diarrhea, depression, lethargy, nose bleed (epistaxis)
- Chocolate given to Dogs and birds can lead to cardiovascular and central nervous system stimulation
- Ethyl glycols (diethylene glycol, ethylene glycol) given to dogs and cats can lead to central nervous system toxicity, nephrotoxicity
- Phenazopyridine in cats can cause hepatotoxicity and red blood cell oxidative injury
- Pseudoephedrine in both dogs and cats can lead to cardiovascular and central nervous system stimulation
- Tobacco products given to dogs and cats can lead to muscle weakness, tachycardia, shallow respiration, collapse, coma, and cardiac failure
- Xylitol given to dogs and birds will cause profound hypoglycemia and hepatocellular necrosis

COMPOUNDING DEFINED BY FDA

- Compounding is defined by the Federal Food, Drug, and Cosmetic Act as any manipulation to produce a dose form of a drug in any form other than what is approved by the FDA.
- Because compounding produces a “new” drug, it is considered drug manufacture and therefore, as with extra-label use, is subject to all regulations for new drugs.
- Veterinary compounders should be knowledgeable of formulations developed specifically for Animal patients

VETERINARY COMPOUNDING

- Formulating drugs with flavored compounds (e.g., fish, beef) so they are more readily accepted by a dog or a cat
- Formulating drugs into capsules or tablets that are no longer available as human drugs (e.g., diethylstilbestrol for urinary incontinence, cisapride for cats with megacolon)
- Formulating drugs into different forms (e.g., gels, pastes, dermatal patches, rectal suppositories) to facilitate administration
- Formulating a raw chemical into a dose form for administration to animals (e.g., potassium bromide reagent used as an anticonvulsant into a syrup or elixir formulation)
EXTRA-LABEL

• Alteration of any of the following from what is described and approved on the drug label is considered extra-label use:
  • Use in a species not listed
  • Use for an indication (disease or condition) not listed
  • Use of a different dosage
  • Use of a different frequency of administration
  • Use of a different route of administration
  • Deviation from labeled withdrawal time (time from last administration of the drug until the animal or the animal’s products can be safely taken to market)

• Guidelines must be followed for use of animal drugs in an extra-label manner.
  • Only a Veterinarian can authorize extra-label use
  • In 1994 Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA) which gave veterinarians the authority to use approved animal drugs in an extra-label manner.

EXTRA LABEL CONT'D.

• Procedures exist to ensure that the identity of the treated animal is carefully maintained.
  • The prescribed or dispensed extra-label drugs bear labeling information that is adequate to ensure the safe and proper use of the product.

• Guidelines must be followed for use of animal drugs in an extra-label manner.
  • In 1994 Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA) which gave veterinarians the authority to use approved animal drugs in an extra-label manner.

THE GOAL OF DRUG THERAPY

• Maintain a drug in the body within the therapeutic range of concentration.
  • The amount of drug entering the body must be balanced by the rate that the drug leaves the body.
    • Pharmacokinetics is the study of how a drug moves into, through, and out of the body.
    • Pharmacodynamics is the study of how the drug produces its effects on the body.

• Different dosage forms exist for four main reasons:
  • Ease of administration and thus compliance
  • Controlled rate of drug delivery
  • Ability to minimize mast or milk withholding times
  • Constraints in treating mating animals

ANIMAL CATEGORIES

• Food
  • Herb or flock animals
  • Residues of drugs must be prevented
  • Vets are required to provide a Withdrawal Drug Time (WDT) that must be present on Rx label

• Companion
  • Cats, dogs, birds, ferrets, gerbils

• Zoo Animals

• Performance Animal
  • Competition animals
    • Horses, dogs
  • Highly regulated by federal and state governments

ANIMAL SPECIES

• One of the primary differences between human and veterinary pharmacology is the wide range of dosage forms available to the veterinarian that occurs as a direct consequence of significant differences in the way drugs are administered to animals and humans.

• These differences are due to the anatomy and physiology of the animal vs. a human, but also due to the behavior and our lack of ability to communicate with them.

• There are at least 24,000 species of fish, 9,000 species of birds, 4,000 kinds of mammals, and 40,000 species of vertebrates.

• The range of veterinary patients varies widely from birds, fish, and small domestic pets to various farm animals, the thoroughbred horse, and the exotic animal species of the jungle or zoological park.

• Different species metabolize medications differently

CAUTION WHEN USING COMMERCIAL PRODUCTS

• Some dosage forms should not be used to compound with:
  • Modified release (extended release, delayed release, repeat action, targeted release)
  • Should not be used unless the suitability for use in a preparation has been documented

• When using solutions the pH of the solution and the pH of the compound should be considered
  • Form
    • Base, Salt, or Ester
SPECIAL ANIMAL DOSAGE FORMS

- Specialized drug delivery devices commonly are used to administer the dosage forms.
  - Esophageal syringes
  - Drench guns
  - Oral tubes designed to deliver medication directly into an animal’s stomach
  - Pole-mounted syringes and projectile delivery systems, which allow injections to be administered from a safe distance
  - Mastitis syringes, for inserting a drug formulation directly into the mammary gland; and others

Other methods for drug delivery include:

- Suspensions
- Transdermal Gels
- Poloxamer Gel
- Chewable treats
- Capsules
- Suppositories
- Solution
- Pastes
- Sterile dosage forms
- Ophthalmic
- Injectable

ESOPHAGEAL SYRINGE


DRENCH GUN

[Image: https://www.agi-pro.com/media/products/60mlDrenchGun_DE53331920DD1_494Dimensions494x301.jpg]

GASTRIC TUBE

[Image: https://horsesidevetguide.com/hsvg/OnlineDatabase/media/651.jpg]

POLE MOUNTED SYRINGE

[Image: http://www.daninject.com/images/daninjectProducts/stick_cow_stick.jpg]

EQUIPMENT AND SUPPLIES NEEDED TO COMPOUND VETERINARY PRODUCTS

- Balances
- Weigh boats/paper
- Capsule Machine
- Capsules
- Balances
- Calibration weights
- Beakers
- Bottles & Caps
- Containers
- Funnel
- Graduates
- Hoods
- Hot Plates
- Molds
- Mortar & Pestle
- Ointment containers/Tubes
- Pipet & Pipettor
- Scoops & Scrapers
- Sealers
- Spatulas
- Spoons
- Stirring Equipment
- Syringe & Accessories
- Thermometers
- Tubes
- Vials
DOCUMENTATION NEEDED

Master Formulation Record
• Record of what should be done
  • The name, strength and dosage form of the preparation
  • Calculations required to determine and verify quantities of all pharmaceutical ingredients
  • Description of all ingredients and their quantities
  • Calculations performed
  • Equipment required to prepare preparation
  • Detailed mixing instructions
  • Sample reporting information, including generic name(s) or trade name(s), identification number, and expiration date of each active ingredient
  • Container and packaging
  • Preparations and formulation of control number
  • Quality control measures and expected results

Compounding Record
• Record of what was done
  • Should be completed for every compound that is prepared
  • Name, strength and dosage form of the preparation
  • MFR reference for the preparation
  • Names and quantities of all components
  • Source, lot numbers, and expiration dates of components
  • Description of the preparation
  • Name of person(s) who prepared the preparation, who performed the quality control procedures, and who approved the preparation
  • Date of preparation
  • Assigned control or RX number
  • Duplicate label
  • Description of final preparation
  • Results of quality control procedures
  • Documentation of any quality control issues and any adverse reactions or preparation problems reported by patient or caregiver.

DOCUMENTATION
• Documentation is needed throughout the compounding process
  • Auditing, tracing, and tracking of dispensed products
  • Quality assurance
  • Assuring reproducibility
  • An MSDS sheet should be kept for every ingredient, and also a Certificate of Analysis should be on file.

CALCULATIONS

To determine a dose for a particular animal, the following elements need to be known:
• The weight of the animal
• The recommended dosage of the drug for animals of this species
• The concentration of the drug

DETERMINE WEIGHT

• Animal’s weight × Conversion factor = Equivalent weight in new units
• Dog’s weight $15\text{ kg} \times 2.2\text{ lb/kg} = 33\text{ lb dog}$

DETERMINE TOTAL DOSE

• Animal’s weight × Dosage Mass of drug
  Body weight = Dose for animal
• 2 kg cat × 50 mg drug
  $\frac{\text{mg}}{\text{kg}} = 100\text{ mg drug}$
• In the event of a dosage range, any number within the range can be used.
  • For example, if a drug has a dosage range of 2 to 4 mg/kg, any of the following would be legitimate doses

DETERMINE QUANTITY OF EACH DOSE

• Dose(Mass) × Volume = Amount of dose from to be given
• Dose(Mass) × tablet = Amount of dose from to be given
• 5 lb animal needs 10 mg of drug, and given that the drug comes in a liquid concentration of 2 mg/mL,
  • 10\text{ mg drug} \times \frac{1\text{ mL}}{2\text{ mg}} = 5\text{ mL of liquid to be given}
**COMPOUND: ANIMAL TREATS FOR DRUG INGESTION**

- Powdered animal food: 13.2 G
- Glycerin: 2 ml
- Flavor (chicken, beef, bacon): 1 ml
- Gelatin base: 6.6 G
- Active drug: qs

Rx makes 3 treats using calibrated dog bone mold add 10% to allow for overfill


**COMPOUND WITH 10% ADDED**

- Set up a formula of \( \text{Want} \) to get a multiplying factor: \( 3 \text{ treats } \times 0.10 = 0.3 = 3 \times 0.11 \)  
  
  - Rx makes 3 treats  
  - Multiplying Factor: 1.1

- Multiply all ingredients by the factor of 1.1
  - Powdered animal food: \( 13.2 \text{ G} \times 1.1 = \) _____________
  - Glycerin: \( 2 \text{ ml} \times 1.1 = \) ______________
  - Flavor (chicken, beef, bacon): \( 1 \text{ ml} \times 1.1 = \) ______________
  - Gelatin base: \( 6.6 \text{ G} \times 1.1 = \) ______________
  - Active drug: qs

**PROCEDURE TO COMPOUND RX**

- Calculate enough product to allow for 10% extra (drug loss)
- Accurately weigh or measure each ingredient
- Cut the gelatin base into small pieces and melt in a beaker using a water bath while melting
- Mix the powdered animal food with active ingredient
- Mix the flavor with the glycerin and add to the melted gelatin
- Incorporate the powdered animal food/active drug mixture with the glycerin in the beaker
- Fill desired molds and allow to harden

**HAIR CONDITIONER FOR HORSES AND OTHER ANIMALS**

- Light liquid petrolatum: 20g
- Aquaphor: 80g

Rx makes 100g

- Rx needed is 30g

- Reduce compound to get amount needed
  - Light Liquid Petrolatum: ______________
  - Aquaphor: ______________


**PROCEDURE TO COMPOUND RX**

- Accurately weigh or measure the calculated quantity of each ingredient
- Using low heat, heat liquid petrolatum in a beaker
- Add Aquaphor and thoroughly mix with stirring rod
- Remove from heat and cool with intermittent stirring
- Package and label

**SULFUR OINTMENT**

- Precipitated sulfur: 10g
- Mineral oil: 10g
- White Ointment: 80g

Compound makes 100g

- Rx needed is 120g for mange

- 120g = 100g

PROCEDURE TO COMPOUND RX

• Calculate the quantity of each ingredient
• Accurately weigh or measure each ingredient
• Levigate the precipitated sulfur with the mineral oil until a smooth paste is formed
• Incorporate the white ointment and mix until uniform
• Package and label

REFERENCES

• https://www.fda.gov/digitalassets/odl-veterinary-drug-interactions-drugs-cats/