Australian and New Zealand College of Veterinary Scientists

Membership Examination

June 2021

Veterinary Pharmacology

Paper 1

Perusal time: **Fifteen (15)** minutes

Time allowed: **Two (2)** hours after perusal

Answer **ALL <u>SIX (6)</u>** questions

Answer **<u>SIX (6)</u>** questions, each worth 20 marks .....total 120 marks

Paper 1: Veterinary Pharmacology

Answer all six (6) questions

1. The metabolic pathways of drug metabolism by the liver can be divided into phase 1 and phase 2 reactions. Describe both pathways and include in your answer the key factors that can affect each pathway. *(20 marks)*

2. Emesis can be humorally or neurally mediated.

   Answer **both** parts of this question:

   a) Outline both the humoral and neural mechanisms of emesis and contrast the relative importance of each mechanism in cats and dogs. *(10 marks)*

   b) Describe the mechanism of action of **two (2)** commonly used medicinal agents in clinical practice that are used to promote emesis in cats and/or dogs. *(10 marks)*

3. Compartment models can be used to describe the pharmacokinetics of drugs that have a measurable rate of distribution from the blood (plasma) to the periphery.

   Answer **all** parts of this question:

   a) Draw a semi-logarithmic plot depicting the concentration over time of a drug displaying two-compartment kinetics after intravenous administration. *(5 marks)*

   b) Draw a schematic diagram of a two-compartment model showing the theoretical movement of the drug through the system after non-intravenous administration. *(5 marks)*

   c) Identify and define the various rate constants included in the two-compartment model you drew for 3 b). *(10 marks)*

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4. Answer **both** parts of this question:

a) Describe the mode of action of a local anaesthetic (LA) of your choice that results in loss of sensation at the site of administration. *(8 marks)*

b) Name and describe the properties of your selected drug that affect the:

i. potency *(4 marks)*

ii. onset of action *(4 marks)*

iii. duration of action. *(4 marks)*

5. Answer **all** parts of this question:

a) Describe the differences between inactivated, modified live and toxoid vaccines, including the advantage(s) and disadvantage(s) of each of them. *(12 marks)*

b) Name **two (2)** commonly used adjuvants in veterinary vaccines and describe the function of each of them. *(6 marks)*

c) In language suited to communications with a farm owner with no scientific background, define the concept of 'herd immunity' and explain how herd immunity protects livestock during a disease outbreak. *(2 marks)*

6. Describe the factors that affect the transdermal delivery of a drug into systemic circulation. Include in your answer the transdermal drug characteristics that enhance the speed of absorption and the bioavailability of a drug delivered to an animal using this route. *(20 marks)*

End of paper

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Paper 2

Perusal time: **Fifteen (15)** minutes

Time allowed: **Two (2)** hours after perusal

Answer **ALL <u>SIX (6)</u>** questions

Answer **<u>SIX (6)</u>** questions, each worth 20 marks .....total 120 marks

Paper 2: Veterinary Pharmacology

Answer all six (6) questions

1. Answer **all** parts of this question:

   a) Define type 1 and type 2 statistical errors and briefly explain their importance in the context of pharmacology. *(5 marks)*

   b) Statistical significance is expressed as the P value. Describe how the P value relates to the types of error described in question 1 a). *(5 marks)*

   c) The abstract on the following page was published in the *Journal of Veterinary Pharmacology and Therapeutics*. A significant difference (P=0.014) was observed for drug terminal half-life between diseased and healthy animals. Explain the meaning of the P-value (P=0.014) obtained in this example. *(5 marks)*

   d) Based on the evidence provided in the abstract, provide brief advice for dairy farmer clients on treatment and withholding period for CEF CFA, when treating diseased animals. *(5 marks)*

Question 1 abstract on following page

Abstract

J Vet Pharmacol Ther 2018 Dec;41(6):848-860. doi: 10.1111/jvp. 12688. Epub 2018 Jul 4.

Comparative plasma and interstitial fluid pharmacokinetics and tissue residues of ceftiofur crystalline-free acid in cattle with induced coliform mastitis.

Gordon PJ[1,2], Ydstie JA[1], Kleinhenz MD[3], Brick TA[1], Smith JS[1], Griffith RW[4], Wulf LW[1,2], Rajewski SM[1,2], Zhang M[5], Sidhu PK[3], Mochel JP[1,6], Coetzee JF[3].

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Abstract

Ceftiofur (CEF) is a third-generation cephalosporin that is the most widely used antimicrobial in the dairy industry. Currently, violative meat residues in cull dairy cattle are commonly associated with CEF. One potential cause for violative residues is altered pharmacokinetics of the drug due to disease, which could increase the time needed for the residue to deplete. The objectives of this study were (a) to determine the absolute bioavailability of CEF crystalline-free acid (CFA) in healthy versus diseased cows; (b) to compare the plasma and interstitial fluid pharmacokinetics and plasma protein binding of CEF between healthy dairy cows and those with disease; and (c) to determine the CEF residue profile in tissues of diseased cows. For this trial, disease was induced through intramammary Escherichia coli infusion. Following disease induction and CEF CFA administration, for plasma concentrations, there was not a significant effect of treatment ($p=0.068$), but the treatment-by-time interaction ($p=0.005$) was significant. There was a significantly greater concentration of CEF in the plasma of the DIS cows at T2 hr ($p=0.002$), T8 hr ($p<0.001$), T12 hr ($p=0.001$), and T16 hr ($p=0.002$). For PK parameters in plasma, the slope of the terminal phase of the concentration versus time curve was significantly lower ($p=0.007$), terminal half-life was significantly longer ($p=0.014$), and apparent volume of distribution during the elimination phase was significantly higher ($p=0.028$) diseased group. There was no difference in plasma protein binding of CEF and interstitial fluid pharmacokinetics. None of the cows had kidney CEF residues above the US tolerance level following observation of the drug's withdrawal period, but one cow with a larger apparent volume of distribution and longer terminal half-life had tissue residues slightly below the tolerance. Whereas these finding do not support the hypothesis that severely ill cows need longer withdrawal times, alterations in the terminal half-life suggest that it is theoretically possible.

KEYWORDS: ceftioful crystalline-free acid, dairy cattle; drug residues; pharmacokinetics

PMID: 29971798 DOI: 10.1111/jvp. 12688

(Indexed for MEDLINE)

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2. Answer **both** parts of this question:

   a) Describe the basic mechanism of action for alkylating agents used in chemotherapy. *(5 marks)*

   b) Select **one (1)** alkylating agent and identify potential side effects associated with this agent. Describe the pathogenesis associated with these side effects and potential actions that could be used to mitigate their severity. *(15 marks)*

3. Describe the physiologic and pharmacologic factors that can affect the rate of induction and recovery from inhalation anaesthesia. *(20 marks)*

4. A farmer has recently purchased a number of mobs of yearling cattle from several suppliers and transported them during summer to a grazing block. Five days after transport, a number of cattle have been heard coughing, with decreased feed intake also noted. Two smaller animals have died. Post-mortem examination revealed pulmonary necrosis and consolidation, with gram-negative bacteria on impression smears from affected tissue. The culture and sensitivity results are pending.

   At the beginning of your response please state the jurisdiction (Australia or New Zealand) pertaining to your responses.

   Answer **both** parts of this question:

   a) List **four (4)** different classes of antibiotics that are available for the empirical treatment of this disease. Give **one (1)** example of an individual antibiotic within each class. *(4 marks)*

   b) Discuss the empirical treatment of affected animals with reference to principles of antimicrobial stewardship and local veterinary regulations. *(16 marks)*

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5. Answer **both** parts of this question:

a) Drug-to-drug interactions are one cause of adverse drug reactions.

Using the headings pharmaceutical, pharmacokinetic and pharmacodynamics, describe these three main categories of drug-drug interactions and give an example for each category.

(5 marks allocated to each category for a total of 15 marks)

b) A German shepherd dog is currently being treated for furunculosis with a veterinary registered formulation of cyclosporin.

As treating veterinarian, you are considering the option of off label use or compounding as a potential way of reducing the cost of medication. Explain how the risk(s) associated with the administration of off label (human prescription/ or compounded) medication in this situation should be communicated to the owner.

(5 marks)

6. A novel oral anticoccidial treatment for use in cattle has been developed.

The product has the following proposed-use pattern claim:

> The product can be used in all classes of cattle from six weeks of age. An oral dose rate of 1 mL/10 kg given daily for five days has been determined in a dose response study. Efficacy studies have demonstrated that the product is highly effective in treating infection and as a preventative treatment when an outbreak occurs. No major adverse events have been identified in residue and efficacy studies. Decreased food intake and minor weight loss were noticed in some animals during these studies.

Describe the additional animal safety studies that would be required to support the proposed-use pattern in order to demonstrate safety for drug registration in New Zealand or Australia for this proposed new product. Include in your answer an overview of the required target animal safety studies, the dose pattern of the product required, and the animals to be selected for these studies. State the jurisdiction (Australia or New Zealand) to which your response applies. *(20 marks)*

End of paper