Feb 21, 2022

Pharmacokinetics and bioequivalence of two imidocarb formulations in cattle after subcutaneous injection

Anonymous [1], Chen Chen[1], Maolin Liu[1], Xiaojie Chen[1], Chunshuang Liu[1], Yanyan Feng[2], Xinbo Yan[3], Yiming Liu[1], Xiubo Li[1], Honglei Wang[1]

[1]National Feed Drug Reference Laboratories, Feed Research Institute, Chinese Academy of Agricultural Sciences, Beijing, China;

[2]Qilu Animal Health Products Corp. LTD Shangdong province, China;

[3]College of Veterinary Medicine, China Agricultural University, Beijing, China

1

dx.doi.org/10.17504/protocols.io.b5c6q2ze

Anonymous

The authors thank farmers in Beijing suburban district for supply with 48 cattle.

Imidocarb (IMD) is commonly used for treatment of eperythrozoon, babesia, piroplasma and trypanosoma in animals, but there are few studies on its pharmacokinetics in cattle. The purpose of this study was to obtain pharmacokinetic parameters and assess the bioequivalence of subcutaneous injections of two IMD formulations in cattle. Forty-eight healthy cattle, 24 males and 24 females, were randomly divided into two groups (test group and reference group) with 12 males and 12 females per group. The generic IMD was injected subcutaneously with a single dose of 3.0 mg/kg in the test group. Reference group animals were given one injection of the marketedIMDat the same dosage. The limit of detection (LOD) and limit of quantification (LOQ) for IMD in cattle plasma were 0.05 μg/Land 0.1 μg/L, respectively. The recoveries ranged from 88.50% to 92.42%, and the equation of this calibration curve was Y=13672.1X+187.43. The pharmacokinetics parameters of the test group showed that the maximum concentration of 2257.5±273.62 μg/L was obtained at 2.14±0.67 h, AUC_{0-t} 14553.95±1946.85 μg·h/L, AUC_{∞}15077.88±1952.19 μg·h/L, $T_{1/2}$ 31.77±25.75 h, CL/F 0.14±0.02 L/h/kg, and V_z/F 6.53±5.34 L/kg. There was no significant difference in AUC_{0-t}, AUC_{∞} and C_{max} between the test group and the reference group (P> 0.05). The 90% confidence interval of AUC_{0-t},$AUC_{0-\infty}$ andC_{max} in the test group was included in 80%–125% AUC_{0-t}, $AUC_{0-\infty}$and 70%–143% C_{max} in the reference group, respectively. Based on these results, the two preparations were found to be bioequivalent.

Citation: Anonymous , Chen Chen, Maolin Liu, Xiaojie Chen, Chunshuang Liu, Yanyan Feng, Xinbo Yan, Yiming Liu, Xiubo Li, Honglei Wang Pharmacokinetics and bioequivalence of two imidocarb formulations in cattle after subcutaneous injection https://dx.doi.org/10.17504/protocols.io.b5c6q2ze

DOI

dx.doi.org/10.17504/protocols.io.b5c6q2ze

Anonymous , Chen Chen, Maolin Liu, Xiaojie Chen, Chunshuang Liu, Yanyan Feng, Xinbo Yan, Yiming Liu, Xiubo Li, Honglei Wang 2022. Pharmacokinetics and bioequivalence of two imidocarb formulations in cattle after subcutaneous injection. **protocols.io**
https://dx.doi.org/10.17504/protocols.io.b5c6q2ze

2016YFD0501305
Grant ID: the National key R & D Program “Drug Resistance Database Construction and Ecological Risk Assessment in Livestock and Poultry Breeding Environment”

Innovation Project of Chinese Academy of Agricultural Sciences
Grant ID: （CAAS-FRI-06)

IMD, Cattle, Pharmacokinetics, Bioequivalence

protocol ,

Feb 21, 2022

Feb 21, 2022

58494

Animals

Twenty-four healthy male cattle and 24 healthy female cattle, aged almost 6 months and weighing 180±15 kg, were selected. The cattle received no treatment for several months prior to the study and were housed in open-air pens. The cattle had free access to water and were fed with a conventional feed without antibiotics during the study. These 48 cattle were divided into 2 groups (test group and reference group) with 24 cattle (12 males and 12 females) in each group. The animals in the test groupwere treated subcutaneously by a single dose injection with a generic IMD formulation, at the recommended dosage 3.0 mg/kg. Animals in the referencegroup were injected subcutaneously with a marketed IMD formulation in the same dose as the test group. All cattle experiment procedures were approved and performed in accordance with the Animal Use and Care Committee of Feed Research Institute, Chinese Academy of Agricultural Sciences （number:FRI-CAAS20150811）. There was no anesthesia and euthanasia in our study. All cattle were alive and healthy after the whole experiment.

Drug formulation

The test drug (the generic IMD, 100 mL:85 mg) was manufactured and provided by Qilu Animal Health ProductsCorp. LTD (Shangdong province, China).

The reference drug (the marketed IMD, 100 mL:85 mg) was manufactured and provided by AKZO-NOBEL Corp. (Boxmeer, Netherlands).

:

The authors thank farmers in Beijing suburban district for supply with 48 cattle.

1 Sample collection

Blood samples (10–15 mL) were collected from the jugular vein at 0 h before administration and 10 min, 30 min, 1, 2, 4, 6, 8, 10, 12, 24, 48, 72 and 96 h after subcutaneous administration, and were drawn in vacutainers containing disodium EDTA as anticoagulant. The samples were immediately centrifuged at 1500 g for 10 min. All the plasma samples in plastic vials were stored at −20°C until they were analyzed.

2 Sample preparation

We used a weak cation-exchange solid phase extraction procedure described by Tarbin [10], and made some modifications to determine the amount of IMD in the plasma. Briefly, 1.0 mL plasma samples were added to plastic centrifuge tubes, adding 3 mL methanol/acetonitrile (90/10, v/v), vertexing for 1 min, ultrasonicating for 15 min, and centrifuging for 10 min at 7000 g. To improve IMD recoveries, the residues were extracted twice. The second extracted solution was combined with the first. The combined extracted solution was passed through SPE columns (Waters Oasis WCX, 3cc 60 mg, Waters Company, USA) conditioned with 3 mL methanol and 3 mL water. The loaded cartridge was washed with 3 mL methanol/water (50/50, v/v), and was eluted with 3 mL methanol/formic acid (96/4, v/v). The analyte was evaporated under a nitrogen stream at 40°C, reconstituted in 1 mL methanol/water (15/85, v/v), and filtered through a 0.22 μm nylon syringe filter before analysis by UPLC-MS/MS.

Citation: Anonymous , Chen Chen, Maolin Liu, Xiaojie Chen, Chunshuang Liu, Yanyan Feng, Xinbo Yan, Yiming Liu, Xiubo Li, Honglei Wang Pharmacokinetics and bioequivalence of two imidocarb formulations in cattle after subcutaneous injection https://dx.doi.org/10.17504/protocols.io.b5c6q2ze