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BII-28

COMPARATIVE *IN VITRO* DERMAL ABSORPTION OF MOXIDECTIN AND DORAMECTIN THROUGH BOVINE SKIN

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Endectocide drugs are used topically to treating ruminant parasitic diseases due to their easy administration, which also avoids residues in an edible administration site. However, available knowledge on their transdermal absorption in cattle is scarce. A practical *in vitro* method to evaluating new topical formulations before *in vivo* assays is not available. The transdermal absorption of moxidectin and doramectin topical formulations was evaluated using an *in vitro* model of bovine epidermis. Epidermal layers (500 µm) were placed on modified Franz diffusion cells. Receptor medium was buffer phosphate (0.1 M), albumin and ethanol (76:4:20). Sampling ranged from 0 to 48 h post-administration. Drug concentrations were quantified by HPLC. By 16.2±6.9 h (MXD) and 33.2± 6.3 h (DRM) post-administration, permeation plateaus were reached. Permeation flows (MXD: 3.8±3.1, DRM: 10.1 ± 8.1 $ng \cdot cm^{-2} \cdot h^{-1}$) differed statistically ($P<0.05$). Permeation coefficients (MXD: $1.6x10^{-06} \pm 1.3x10^{-06}$ cm/h, DRM: $4.12x10^{-06} \pm 3.44x10^{-06}$ cm/h) were similar ($P>0.05$). These results agree with the faster plateau and shorter T_{lag} of MXD (2.4± 0.6 h) compared to DRM (12.2 ± 5.4 h), which could be due to different lipophilicity. Results are in agreement with *in vivo* kinetic data. The *in vitro* m**odel** presented here is useful to predicting and further understanding of endectocides' transdermal absorption process in cattle**.**

BII-29

EFFECTIVENESS OF ENHANCERS' COMBINATION ON TRANSDERMAL PERMEATION OF PROBENECID.

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The pharmaceutical design is a very complex field due to the existence of multiple forms of administration. The oral route presents some disadvantages such as gastric irritation, exposition of the drug to extreme pH and degradation by hepatic first pass. A non-invasive alternative to avoid these effects are the transdermal formulations, which present the advantage to release the drug in constant and prolonged way. Nevertheless the transdermal drug administration itself is limited by the characteristics of the skin, which offers a remarkable resistance to the penetration of the active principles. Therefore, it is necessary to include in the formulations chemical compounds that, by different mechanisms, facilitate the penetration of the drug. In this study, using Franz diffusion cells, *in vitro* transdermal permeation of probenecid (uricosuric drug) in solid vaseline through dermatomized pig skin was assayed. Also, the isopropyl alcohol action and their combinations with terpene enhancers (L-menthol or D-limonene) were investigated. The obtained results allow to determine that isopropyl alcohol increases 5-fold the diffusion coefficient value ($D = 2.022 \times 10^{-7}$ cm^2/s) in relation to the formulation without enhancer ($D = 3.998 \times 10^{-8}$ cm^2/s). The addition of L-menthol or D-limonene to the formulation containing isopropyl alcohol increases 4-fold, approximately, its diffusion coefficient value. This fact shows the existence of a synergic effect between these terpenes and isopropyl alcohol.

BII-30

CHRONOKINETIC STUDY OF INTRAMUSCULAR ADMINISTRATION OF CEFTAZIDIME IN DOGS

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The purpose of this study was to identify if time of day administration modified ceftazidime relevant pharmacokinetic parameters administered to dogs. Six healthy female mixed breed adult dogs weighing 14-22 kg were given a single 25 mg/kg dose of ceftazidime by the intramuscular route at 8.30 and 20.30 h after an 8 h fast, with a 2 week washout period. Blood samples were taken at predetermined times. Concentrations of ceftazidime were determined by microbiological assay. Data were analysed by noncompartmental techniques using PCNONLIN software. Results are reported as mean ± standard deviation. For the 8.30 h administration, peak concentration, time to peak concentration and elimination half-life were 80.2 ± 20.7 µg/ml, 1 ± 0.27 h and 1.13 ± 0.30 h, respectively. For the 20.30 h administration, peak concentration, time to peak concentration and elimination half-life were 104.30 ± 24.98 µg/ml, 0.75 ± 0.44 h and 1.1 ± 0.33 h, respectively. No statistically significant differences were detected for all the pharmacokinetic parameters, however, high standard deviations may have accounted for this lack of difference. Our data suggest that time of administration may not modify the pharmacokinetics of intramuscular ceftazidime in dogs.

BII-31

ORAL ABSORPTION OF CEPHALEXIN ADMINISTERED IN DAY-TIME, NIGHT-TIME AND AFTER METOCLOPRAMIDE IN DOGS

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The purpose of this study was to compare if the time of administration or metoclopramide pretreatment modified the absorption of cephalexin after its oral administration to dogs. Six healthy adult Beagle dogs weighing 9-13 kg received a single dose (25 mg/kg) of cephalexin as a 5% oral suspension at 10.00 h (day-time) or 22.00 h (night-time) and also 5 min following the intravenous administration of metoclopramide (0.5 mg/kg) after 8 h fasting period. Blood samples were taken at predetermined times. Cephalexin plasma concentrations were quantified by a microbiological method with *Micrococcus luteus* 9341 ATCC as test microorganism. Mean cephalexin concentrations for each treatment were used to evaluate the absorption process by the Wagner-Nelson method. Results showed a first-order absorption process for the three treatments. Statistically significant differences were detected for the regression line slope of log-unabsorbed fraction of cephalexin versus time. Absorption rates were 1.06, 1.75 and 1.54/h for the 10:00 h-treatment (day-time), 22:00 h-treatment (night-time) and after metoclopramide pretreatment, respectively. Absorption times were 3.5 h (day-time), 2.5 h (night-time) and 1.5 h (metoclopramide pretreatment). Our results show that the moment of administration and also metoclopramide pretreatment affected cephalexin oral absorption in dogs.