BIOEQUIVALENCE OF IVERMECTIN FORMULATIONS IN BEEF CATTLE

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Introduction

Ivermectin is a broad spectrum endectocide used extensively in small animals as well as large animals. Its abundant use has resulted in increasing productions of generic products once the original product patent expired. The efficacies of these generic products need to be evaluated according to standard international guidelines (EMEA 2001, FDA 2006). This study, thus was aimed to investigate bioequivalence of a test product (Vermax/ VM) and the original product (Ivomec®/ IVM) following subcutaneous injection into beef cattle.

Materials and Methods

Eighteen healthy Native-Indu Brazil crossbred beef cattle were divided into 2 groups of nine animals. The experiment design was a single two-period cross-over design. In each period, they were subcutaneously injected with either IVM or VM at 200 µg/kg body weight. Blood samples were collected at 0, 0.25, 0.5, 0.75, 1, 2, 4, 8, 12, 16, 24, 36h, and at 2, 3, 4, 5, 6, 8, 10, 15, 20, 25, 30, and 35 days post-injection. Plasma was separated after centrifugation blood samples at 3000 rpm for 15 minutes and stored at -20°C until analysis. Each plasma sample was extracted and derivatized using a method described in details elsewhere (Alvinerie et al. 1993, Alvinerie et al. 1995, de Montigny et al. 1990). All derivatized samples were injected to a High Performance Liquid Chromatography (HPLC) system equipped with a fluorescence detector to determine plasma concentration of ivermectin. The excitation and emission wavelengths were 365 and 475 nm, respectively.

Results and Conclusion

Figure 1 Average plasma concentration of 2 ivermectin formulations: Ivomec®(IVM) and Vermax (VM) following subcutaneous injection in beef cattle (n =9 in each group).

The ivermectin was detected in animal plasma up to 20 days post-injection of both formulations (Figure 1). The peak plasma concentrations (C<sub>max</sub>) of IVM and VM were 231.3 ± 46.4 and 219.6 ± 27.0 ng/mL, respectively. The area under the concentration-time curve of IVM
and VM from day 0-20 (AUC$_{0-20d}$) were 24953 ± 4035 and 26403 ± 1741 ng-hr/mL, in order. There were no significant differences in measured pharmacokinetic parameters between the two formulations. This indicated that both IVM and VM were bioequivalent following subcutaneous administration at 200 µg/kg body weight and can be used interchangeably.

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References