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VITAMIN K ABSORPTION IN THE HORSE: INTESTINAL UPTAKE OF DIFFERENT VITAMERS

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Vitamin K has recently been found to be involved in many physiological processes beyond that of blood coagulation. 14 vitamin K-dependent proteins (to date) have now been identified, with essential roles bone metabolism, innate immune system and controlling arterial calcification . Current research has focused on the metabolism of vitamin K and human osteoporosis, with limited research on bone disease in horses. There are a number of forms of vitamin K [phylloquinone (K1), that is synthesized by green plants: menaquinones (MKs also known as K2) synthesized by bacteria; menadione (K3) is the synthetic form of the vitamin and is routinely added to animal diets] but there is no consensus of their efficacy *in vivo.* As absorption is the first step in vitamin K metabolism, the objective of this study was to determine the absorption efficiency of different isoforms of vitamin K in the horse.

Twelve mature geldings were paired and allocated to six groups in a random crossover design. Sampling was undertaken over six experimental periods. There were six treatments consisting of a control, K1, K2 (in the form of MK-4), K3 and KQ (QAQ; Quinaquanone™ a soluble form of K1 and K2 (10:1). These were administered as a 200mg oral bolus (suspended in water) to each horse. Blood sampling was undertaken at designated intervals for 480min. In the last treatment K1 (200mg) was administered intravenously into the right jugular vein and blood samples collected at designated intervals for two hours. Plasma samples for each treatment were then analysed by HPLC for K1, MK-4 and K3 concentrations.

Plasma K1 concentrations differed significantly across time and between treatments ($p<0.001$) with the highest plasma K1 concentrations occurring with the KQ treatment compared to the other treatments ($P>0.0001$), with K1 peaking second highest. Both KQ and K1 showed no detectable conversion to K3 (menadione) or MK4 in plasma. Moreover, the administration of K3 showed that plasma K3 was well absorbed, but there was no detectable conversion to MK4 in plasma. Pharmacokinetic parameters [area under the curve (AUC), time to maximum (t*max)* and maximum concentration (C*max)*] were derived for each treatment and bioavailability calculated for oral treatments relative to K1 administered intravenously (100%). The bioavailability was 0.45% for QAQ, 0.14% for K1.

The results of this study clearly demonstrate that the horse appears to almost exclusively have K1 in plasma in contrast other species .. This suggests that there is no specific conversion of K1 to K3 or K3 to MK-4 in plasma in the horse, contrary to what occurs in some other mammals (rat and human). In the species vitamin K1 is converted in the liver to K3, and plasma K3 is prenylated in the tissues to MK4.The soluble form of the vitamin, KQ was the most efficiently absorbed and should be evaluated in further studies that examine metabolism of vitamin K in the horse, especially bone metabolism.