Characterize and Compare the Oral Pharmacokinetics of Luteolin in Mini Pigs and Beagle Dogs

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Objectives: To characterize and compare the pharmacokinetics of luteolin in mini pigs and Beagle dogs using nonlinear mixed-effects modeling (NONMEM).

Methods: Luteolin is a natural polyphenol (flavonoid) found in plants and one of major bioactive component of chrysanthemum morifolium extract (CME). As reported in the literature, many flavonoids exhibited various pharmacological effects, such as antioxidant, anti-inflammatory, anti-mutagenic, and anti-allergic activities. In this study, the plasma concentrations of luteolin were determined in both mini pigs and Beagle dogs following oral administration of CME. Pharmacokinetic (PK) modeling was performed using NONMEM. The final model was selected based on the likelihood ratio test using objective function values and graphical goodness-of-fit.

Results: The PK profiles of luteolin in both mini pigs and Beagle dogs were best described by a one-compartment model with first-order absorption and a proportional error model. The population means (SE) of the absorption rate constant (KA), the apparent clearance (CL/F), and the apparent volume of distribution (V/F) were 0.14 (0.03) hr⁻¹ and 2.18 (0.94) hr⁻¹, 1.78 (0.31) L/hr and 1.34 (0.14) L/hr, and 5.15 (1.21) L and 16.5 (0.61) L for mini pigs and Beagle dogs, respectively. It appears that luteolin has a relatively slower absorption and lower V/F in mini pigs compared to Beagle dogs, while the CL/F values appear similar in the two species.

Conclusions: The PK model developed in this study adequately characterizes the absorption, distribution, and elimination of luteolin in both mini pigs and Beagle dogs.