

The Gastrointestinal System and Oral PK in Göttingen Minipigs

The pig is an omnivore and has a digestive physiology very similar to that in humans. Accordingly, Göttingen Minipigs have been used in nutritional studies; in some cases, fitted with re-entrant fistulas to study regional intestinal digestion.¹ The comparative biology of the gastrointestinal system in Minipigs and humans, including specific anatomic differences, have been thoroughly described elsewhere.²⁻⁵ The characteristics of the different segments of the gastrointestinal tracts (i.e. size, pH, etc.) are nicely summarized by Suenderhauf et al.⁴

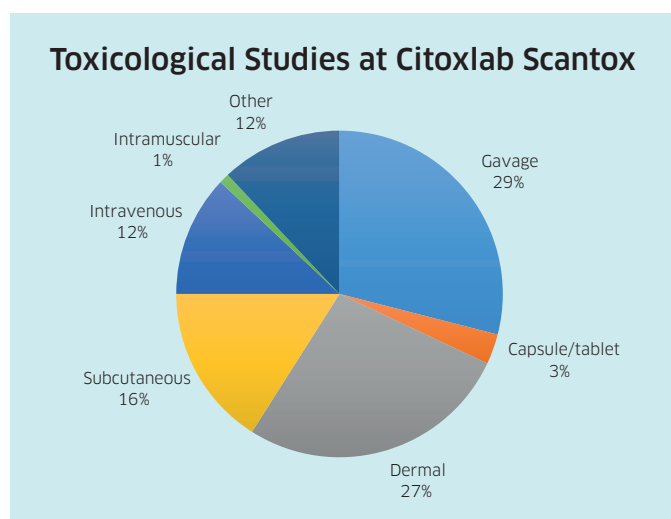
As a reflection of the clinical situation, the oral route of administration is the most commonly used in toxicology studies (see the illustration below). There are several ways of dosing orally in Göttingen Minipigs but in toxicology studies, the compound is usually given by gastric lavage using a volume of 2-10 ml/kg - in accordance with the administration volumes considered good practice.⁶ A dosing chair, as the one described in Newsletter No. 47 (for download at www.minipigs.dk), can be of help and depending on the technique used and the size of the Minipigs, two to three persons are usually involved in dosing a group of Minipigs.

The gastric pH in the fasted Minipig is less variable and more comparable to that in humans than in the fasted dog (where it is

often basic).^{4,5,7} The gastric emptying of the Minipig is, however, slower than the gastric emptying observed in humans.^{8,9} By removing the straw bedding (and potentially replacing it with other enrichment types), the stomach content remaining after an overnight fast can be markedly reduced.⁸ In such a setting, mean gastric transit times were 0.63 h, 1.36 h, and 0.73 h for solution, capsules and tablets, respectively.⁸ Other studies evaluating gastric emptying and food effects on oral drug absorption used Minipigs kept on straw bedding throughout the study,^{9,10} a factor which likely influenced the findings in those studies.

The tolerability to many compounds is higher and more human-like in Göttingen Minipigs than in the dog. For instance, dogs show excessive vomiting in response to many compounds, including anticancer compounds,¹¹ and have a low tolerance to NSAIDs, that tend to result in gastrointestinal lesions.³

A recent review presented data demonstrating the suitability of the pig as a preclinical model to predict human oral bioavailability (with slightly better performance than the dog).⁵ The overall similarity between humans and Minipigs regarding intestinal transporters and metabolizing enzymes in the intestine and liver,^{5,12} helps to explain this finding.



“Over the years, the large number of toxicological studies performed in Göttingen Minipigs at Citoxlab in Denmark have involved many different routes of administration. The oral dosing route is the one most commonly used, and one that we have good experience with.” Andy Makin, Scientific Director, Citoxlab Denmark

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