corresponding times, where slope equals Kel. $t_{0.5}$ was then calculated using the following equation $t_{0.5}$ = 0.693/ Kel which is defined as the time required for a drug to fall half of its initial value.

Statistical analysis

Statistical comparisons were obtained using one-way ANOVA followed by Tukey's to compare between more than two groups using SPSS statistical software, (IBM, USP); version 22. Each data point represents the mean ± SEM. P-value less than 0.05 was considered statistical significant ($p<0.05$).

2.2.5.4 Data analysis (Optimized effective intestinal permeability)

Effective intestinal permeability (P_{eff}) values were estimated by Nelder–Mead algorithm of the Parameter Estimation module using SimCYP program. The Nelder–Mead method, which is also called downhill simplex, is a commonly used nonlinear optimization algorithm. This was done by searching for the best parameter values that produce plasma concentration that matches the actual plasma concentration at the same time. The objective function is the weighted sum of squared differences of observed and model predicted values. Polar surface area was used first to predict an initial estimate of P_{eff}. SimCYP program was used under academic license from SimCYP Ltd, Sheffield, U.K. (Lic. # CLCLID – AKDI – LEEE – FECI).

2.2.6 Anaesthesia and surgical protocol

A perfusion system consisting of an anaesthesia system (SomnoSuite small Animal Anesthesia System, Kent Scientific Corporation Torrington, USA) that is linked to an oxygen