distributed to all tissues. The oral bioavailability of diacerein is approximately 3-fold that of rhein (Louchahi et al., 1991). Absolute bioavailability of the oral form of diacerein is unknown due to absence of an injectable form.

In order to estimate bioavailability, urinary elimination profiles are implemented. Nonetheless, biliary excretory pathway cannot be excluded as 20-25% of the elimination of rhein occurred via the bile following a dose of 25 mg/kg diacerein in rats.

Pharmacokinetics of diacerein can be estimated through plasma concentrations of rhein as diacerein itself is not detectable in biological fluids after oral administration to humans where each 100 mg diacerein contains 77.2 mg rhein.

Following a single oral dose of diacerein (50 mg) to 12 healthy volunteers, maximum plasma concentration (Cmax) of rhein was 3.15 mg/l at 2.4 hours after administration (Louchahi et al., 1991). The AUC0-∞ was 20.9 mg/l.h, terminal elimination half-life ($t1/2\beta$) was 4.25 hours and renal clearance (Clren) was 0.12 l/h. Mean oral bioavailability after a single administration of a 50 mg dose was 34.7±11.9% using cumulative 24-hour urinary excretion.

In the same study, multiple dosing (50 mg twice daily for five days) generated a 38% higher AUC than single dosing. The Cmax after multiple dosing was 30% higher than expected from Cmax after the single dose multiplied by the accumulation factor. The unexpectedly high values for Cmax and AUC after multiple dosing were due to a miscalculated mean t1/2 of only 4.25 hours because of an inadequate 24 hour blood sampling period. If sampling had been extended to 48 hours, the correct half-life (7.2–7.8 hours) would have been identified. Using this value, the theoretical Cmax is in good accordance with the experimental value reported after multiple dosing.