

**Disposition of Radioactivity 72 Hours Following Oral Gavage Dose
of 100 mg/kg [¹⁴C]Kawain to Male F-344 Rats Following Repeat Administration of
Kava (Normalized to 100 mg/kg Kavalactones) for 7 Days (Group 4)^a**

Dose Recovered in Excreta (%)

| End of Collection Period (h) | Urine CPDE ^b | Feces CPDE | Total CPDE |
|------------------------------------|----------------------------|---------------|---------------|
| 8 | 39.0 ± 3.2 | c | 39.0 ± 3.2 |
| 24 | 68.4 ± 1.1 | 6.32 ± 2.4 | 74.7 ± 2.5 |
| 48 | 74.7 ± 1.4 | 13.5 ± 2.3 | 88.2 ± 2.4 |
| 72 | 77.3 ± 1.5 | 14.6 ± 1.8 | 91.9 ± 2.2 |

Distribution in Tissues (72 hours)

| Tissue | ng-eq Kawain per g Tissue | Tissue/Blood Ratio | % Dose in Total Tissue |
|-------------------------|------------------------------|-----------------------|---------------------------|
| Adipose | 468 ± 165 | 0.517 ± 0.211 | 0.0437 ± 0.0151 |
| Blood | 933 ± 90.0 | Unity | 0.0610 ± 0.00651 |
| Brain | 39.3 ± 3.83 | 0.0422 ± 0.0022 | 0.0003 ± 0.00003 |
| Heart | 265 ± 24.4 | 0.284 ± 0.0094 | 0.0008 ± 0.0001 |
| Kidney | 2360 ± 101 | 2.55 ± 0.238 | 0.0180 ± 0.00116 |
| Liver | 3350 ± 376 | 3.61 ± 0.395 | 0.128 ± 0.0138 |
| Lung | 405 ± 30.8 | 0.436 ± 0.0411 | 0.00161 ± 0.000238 |
| Muscle | 108 ± 8.81 | 0.117 ± 0.0181 | 0.0386 ± 0.00282 |
| Skin | 613 ± 91.7 | 0.666 ± 0.149 | 0.103 ± 0.0143 |
| Total in Tissues | — | — | 0.395 ± 0.032 |

^aAll values expressed as mean ± standard deviation (SD) (N = 4). Kawain is a constituent of kava extract (kava). The target dose was 100 mg Kawain/g body weight and was administered as a single dose following 7 days of dosing with kava normalized to 100 mg kavalactones/kg body weight. Kava extract contains ca. 40% kavalactones of which the major constituents (96%) are 5,6-dehydrokawain; 7,8-dihydrokawain; 7,8-dihydromethysticin; kawain; methysticin; and yangonin.

^bCPDE = Cumulative percent dose excreted.

^cThe first feces collection was at 24 hours (h).