In vivo pharmacokinetic and tissue distribution studies of a natural anticancer diterpene isolated from *Caesalpinia pulcherrima*

S. D. V. Gunawardane, E. A. Oshadi, P. K. S. Wijerathne, P. A. N. Punyasiri, K. S. Senathilake, U. Rajagopalan, S. R. Samarakoon

Institute of Biochemistry, Molecular Biology and Biotechnology, University of Colombo, Sri Lanka

A cassane-type diterpene, 6β-Cinnamoyl-7α-hydroxyvouacapen-5α-ol (DC3B), is isolated from *Caesalpinia pulcherrima* and has demonstrated promising *in vitro* anticancer potential. This study aimed to evaluate the pharmacokinetics and tissue distribution of DC3B in male Wistar rats. A reverse-phase high-performance liquid chromatography method (RP-HPLC/UV) was developed and validated according to the United States Food and Drug Administration (US FDA) guidelines for bioanalytical method validation, using a C18 column with a methanol-water gradient and UV detection at 275 nm. DC3B and the internal standard (propyl paraben) eluted at 8 and 4 min, respectively. The RP-HPLC method was fully validated for specificity, selectivity, linearity ($R^2 > 0.999$), sensitivity, accuracy, precision, extraction recovery, matrix effect, carryover, and dilution integrity across all matrices. The validated HPLC method was applied to quantify DC3B in rat plasma and tissues. DC3B was administered orally at a single dose of 200 mg/kg using corn oil as the vehicle. Plasma and tissue samples were collected at 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 16, and 24 h post-dose. The compound was absorbed with a T_{max} of 4 h, a C_{max} of 1314.12 ± 31.41 ng/mL, and a plasma elimination half-life ($t_{½}$) of 1.37 h in plasma. DC3B was distributed to major organs, with peak concentrations (C_{max}) observed in the liver (1752.41 ng/mL), stomach (27549.02 ng/mL), small intestines (23377.15 ng/mL), lungs (1139.84 ng/mL), kidneys (702.47 ng/mL), heart (1807.90 ng/mL), and spleen (704.56 ng/mL). Notably, DC3B penetrated sanctuary sites such as the brain and testes, with C_{max} of 408.94 and 2881.99 ng/mL, respectively. Although DC3B exhibited delayed absorption, it demonstrated substantial and widespread tissue distribution. Its accumulation in the above organs highlights its capacity to reach protected or metastatic niches, reinforcing its potential as a cancer stem cell-targeting agent. These findings support oral administration as a viable route and underscore the need for formulation and dosing strategy refinements to improve systemic exposure and therapeutic outcomes.

Keywords: *Cassane diterpene, Caesalpinia pulcherrima, Pharmacokinetics, Tissue distribution, RP-HPLC/UV*