Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **29** (3): 428-435 (2010)

Original Article

Received: September 12, 2009
Accepted: October 15, 2009

Pharmacokinetics, Tissue Distribution and Bioavailability of Imatinib in Mice after Administration of a Single Oral and an Intravenous Bolus Dose

Magdalene TEOH, Shantini RADHAKRISHNAN, Kai S. MOO, Prasad NARAYANAN, Nadeem I. BUKHARI & Ignacio SEGARRA *

Department of Pharmaceutical Technology, School of Pharmacy & Health Sciences, International Medical University, No. 126 Jalan 19/155 B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

SUMMARY. **Imatinib inhibits Bcr-Abl, c-KIT and PDGFR kinases involved in chronic myelogenous leukemia and gastrointestinal stromal tumors. Mice were given imatinib PO (50 mg/kg) or IV (12.5 mg/kg) and plasma, liver, brain, spleen, kidney disposition profiles analyzed. Plasma $t_{1/2}$ was 4.5 h. IV plasma $AUC_{0\rightarrow\infty}$ was 11.59 μg·h/mL, MRT was 4.87 h, Cl was 1.08 l/h/kg and V_{SS} was 5.23 l/kg. PO $AUC_{0\rightarrow\infty}$ was 12.82 μg·h/mL, MRT 5.1 h, C_{MAX} was 6.99 ± 2.84 μg/mL, absorption rate constant, K_a was 4.348 h^{-1}, bioavailability was 27.7%, V_{SS} was 5.51 l/kg. The hepatic extraction ratio was 0.384 and the minimum dose fraction absorbed was 0.450. IV $AUC_{0\rightarrow\infty}$ tissue-to-plasma ratios were 2.59 (spleen, kidney) and 2.91 (liver) but increased after PO administration in spleen (3.68) and kidney (3.49) and decreased in liver (2.75). Liver and kidney correlations with plasma concentrations suggests perfusion-limited uptake. Spleen counter-clockwise profile suggests non-concentration dependent uptake. Brain penetration was minimal.**

KEY WORDS: bioavailability, chronic myeloid leukemia, gastrointestinal stromal tumor, imatinib, pharmacokinetics, tissue distribution.

* Author to whom correspondence should be addressed. *E-mail:* segarra100@gmail.com

ISSN 0326-2383