



**Effect of the ET(B) receptor agonist, IRL-1620, on paclitaxel plasma pharmacokinetics of breast tumor rats.**

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Endothelin (ET)-B receptors are expressed in human breast carcinoma. We previously demonstrated that intravenous administration of the ET(B) receptor agonist, IRL-1620, to tumor-bearing rats, increased blood perfusion and enhanced delivery of paclitaxel to breast tumor tissue. The present study was conducted to determine whether IRL-1620 alters the pharmacokinetics of paclitaxel. Breast tumor-bearing rats were given 0.3 ml/kg saline or 3 nmol/kg IRL-1620 by intravenous (iv) administration. Fifteen minutes after saline or IRL-1620, 40 microCi/rat <sup>3</sup>H-Paclitaxel was administered iv and serial plasma samples were collected until 24 hrs. <sup>3</sup>H-Paclitaxel radioactivity in the plasma samples was measured by liquid scintillation counting. Data were fit to a three-compartment model and pharmacokinetic parameters were generated using WinNonlin software. IRL-1620 did not produce any change in the plasma paclitaxel pharmacokinetics of tumor-bearing rats. The AUC(0-infinity) (9.43 +/- 3.18 microg-hr/ml), clearance (0.69 +/- 0.17 l/hr/kg), volume of distribution (10.31 +/- 4.54 l/kg), and half-life (1.0 +/- 0.32 hrs) of paclitaxel were similar between rats treated with saline or IRL-1620. In conclusion, the ET(B) receptor agonist, IRL-1620, does not alter paclitaxel plasma pharmacokinetics and, therefore, could be used to augment the delivery of paclitaxel to the tumor tissue.