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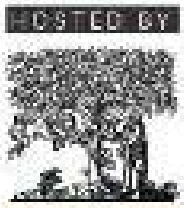

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ORIGINAL ARTICLE

Preclinical investigation of the pharmacokinetics, metabolism, and protein and red blood cell binding of DRDE-07: a prophylactic agent against sulphur mustard

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Abstract DRDE-07, a newly synthesized amifostine analog currently under clinical investigation in a phase I trial, is a potent antidote against sulfur mustard toxicity. The purpose of this research was to evaluate the pharmacokinetic profile of DRDE-07 in female Swiss Albino mice after a single oral dose of 400 or 600 mg/kg. The physicochemical properties of DRDE-07, including solubility, pK_a, Log *P*, plasma protein binding and plasma/blood partitioning, were determined to support the pharmacokinetic characterization. DRDE-07 concentration was determined by an HPLC-UV method. The profile of plasma concentration versus time was analyzed using a non-compartmental model. Plasma protein binding was assessed using ultrafiltration. DRDE-07 appeared rapidly in plasma after oral administration with peak plasma levels (C_{max}) observed in less than 15 min. There was a rapid decline in the plasma levels followed by a smaller second peak about 90 min after dosing. The plasma protein binding of DRDE-07 was found to be less than 25% at all concentrations studied. Plasma clearance of DRDE-07 is expected to be ~1.5 fold higher than the blood clearance of DRDE-07. The probable metabolite of DRDE-07 was identified as phenyl-*S*-ethyl amine.

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