Toxicity evaluation of oral docetaxel granule

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Abstract

Oral administration of chemotherapy drugs is highly favored due to its convenience, yet many drugs, like Docetaxel (DTX), face challenges due to poor solubility and permeability, necessitating intravenous delivery. DTX, a potent microtubule inhibitor used widely in cancer treatment, is highly lipophilic and water-insoluble, requiring the addition of 50% polysorbate 80 in commercial injections, potentially causing hypersensitivity reactions. Understanding maximum tolerated dose (MTD) and toxicity is crucial in preclinical and clinical settings, yet these parameters remain unexplored for oral DTX formulations. Our previous work developed an oral DTX granule, showing promising tumor growth inhibition. This study systematically assesses MTD, tissue distribution, and toxicity of oral DTX granule in mice. We found sex-specific differences in toxicity and absorption, with MTD set at 50 mg/kg for females and 25 mg/kg for males. Interestingly, females exhibited higher tissue absorption. At an elevated dose (400 mg/kg), kidney damage was observed without impacting liver and lung tissues. These findings furnish foundational insights for future preclinical investigations and clinical translation of oral DTX formulations in cancer therapy.