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Modulation of bioavailability of anticancer drugs by Drug interactions: An update

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There has been increasing interest in the oral delivery of anticancer agents in chronic therapy, for patient convenience and ease of administration. Oral bioavailability of many anticancer drugs is poor and highly variable. This is a major impediment to the development of new generation drugs in oncology like farnesyl transferase inhibitors. Limited bioavailability is mainly due to: (1) cytochrome P450 (CYP) activity in gut wall and liver, and (2) drug transporters, such as P-gp in gut wall and liver. Blockers of P-gp can drastically improve oral bioavailability of paclitaxel and other drugs in mice and humans. The taxanes, paclitaxel and docetaxel are considered excellent substrate drugs to test the concept that by inhibition of P-gp in the gut wall and CYP activity in gut wall and/or liver low oral bioavailability can be increased substantially. The increase in bioavailability of tamoxifen is likely to be due to the decrease in first-pass metabolism in the intestine and liver by inhibition of P-glycoprotein and CYP3A by EGCG. Food-drug interactions can have four pharmacokinetic effects on the bioavailability of the orally administered anticancer agent: delayed, decreased, increased or unaffected absorption. For example, both delayed and decreased absorption of chlorambucil in the fed rather than the fasting state due to the slowed rate of gastric emptying. In addition, chlorambucil is unstable and undergoes hydrolysis in gastric fluid. Some orally administered anticancer agents (like capecitabine, altretamine and estramustine phosphate sodium) are prodrugs, which require metabolic activation. A decrease in the rate and extent of absorption is noted when estramustine phosphate sodium is given with food or milk, and bioavailability has been reported to decrease by 36% and 63%, respectively, opposite is for fluorouracil (5-FU). Dose-dependent CYP inhibition has been observed following administration with grapefruit juice, affecting the bioavailability of anticancer agents. The consideration of food and drug-drug interactions effects is important every time he/she prescribes a new drug, as it could lead to more rational pharmacological monitoring and possibly improve the oral chemotherapy of cancer.

Biography

Dr. Sanjita Das has completed her PhD and M.Pharm in Pharmacology from Birla Institute of Technology. She is the Head of the Department of Pharmacology, Noida Institute of Engineering and Technology, Greater Noida, India. She has published 26 publications in reputed Journals an as serving as an editorial board member of repute. She has worked as a reviewer for many reputed journals. She is guiding six PhD scholars. She is a member of Indian Pharmacology Society, Indian Chemical Society, Indian Pharmaceutical Association, Indian Pharmaceutical Graduates Association, Association of Pharmaceutical Teachers of India, and Indian Technical Society. Now she is involved in exploitation of medicinal values of the traditionally used plant sources and bioavailability studies of different medicinal products.