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The use of oral anticancer drugs has increased during the last decade, because of patient preference, lower costs, proven efficacy, lack of infusion-related inconveniences, and the opportunity to develop chronic treatment regimens. Oral administration of anticancer drugs is, however, often hampered by limited bioavailability of the drug, which is associated with a wide variability. Since most anticancer drugs have a narrow therapeutic window and are dosed at or close to the maximum tolerated dose, a wide variability in the bioavailability can have a negative impact on treatment outcome. This review discusses mechanisms of low bioavailability of oral anticancer drugs and strategies for improvement. The extent of oral bioavailability depends on many factors, including release of the drug from the pharmaceutical dosage form, a drug's stability in the GI tract, factors affecting dissolution, the rate of passage through the gut wall, and the presystemic metabolism in the gut wall and liver. These factors are divided into pharmaceutical limitations, physiological endogenous limitations, and patient-specific limitations. There are several strategies to reduce or overcome these limitations. First, pharmaceutical adjustment of the formulation or the physicochemical characteristics of the drug can improve the dissolution rate and absorption. Second, pharmacological interventions by combining the drug with inhibitors of transporter proteins and/or presystemic metabolizing enzymes can overcome the physiological endogenous limitations. Third, chemical modification of a drug by synthesis of a derivative, salt form, or prodrug could enhance the bioavailability by improving the absorption and bypassing physiological endogenous limitations. Although the bioavailability can be enhanced by various strategies, the development of novel oral products with low solubility or cell membrane permeability remains cumbersome and is often unsuccessful. The main reasons are unacceptable variation in the bioavailability and high investment costs. Furthermore, novel oral anticancer drugs are frequently associated with toxic effects including unacceptable GI adverse effects. Therefore, compliance is often suboptimal, which may negatively influence treatment outcome.

Release

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The development of preexposure prophylactics or microbicide products for the reduction or elimination of the sexual transmission of HIV has numerous challenges or barriers to success. Historically traditional dosage forms such as gels have been developed in the field but more recently controlled release dosage forms such as vaginal rings and novel dosage forms such as polymeric thin films have been studied. Studies have begun to incorporate scientific strategies into the formulation design of microbicide products in order to develop safer and more effective products. In addition, advanced drug delivery strategies to overcome barriers to delivery and specific drug targeting methods are being employed. In the present review, a comprehensive discussion of formulation efforts and novel delivery strategies in the field of microbicide product development is presented.