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Nanotechnology approaches for oral bioavailability enhancement of drugs undergoing extensive hepatic first pass metabolism

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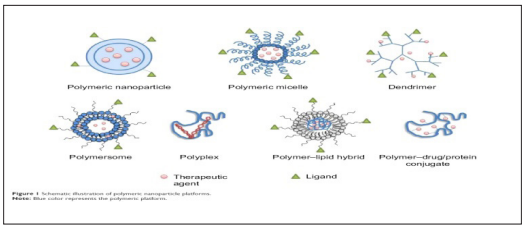

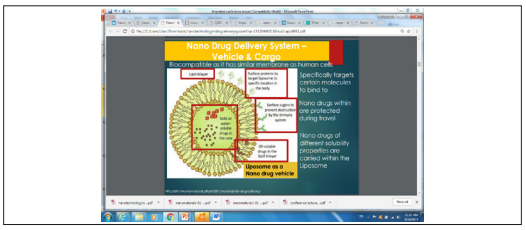

Oral administration is the most convenient route among various routes of drug delivery as it offers high patient compliance. However, the poor aqueous solubility and poor enzymatic/metabolic stability of drugs are major limitations in successful oral drug delivery. Extensive hepatic first pass metabolism is one of the principal reasons for poor oral bioavailability of drugs. It is a mechanism whereby detoxification of drugs and their conversion to their water-soluble forms occurs which facilitates convenient excretion through kidneys. However, it prevents required amounts of the drug to reach systemic circulation leading to a need of higher doses to achieve minimum effective plasma concentrations. This results in dose related side effects and thus poor patient compliance. The resulting metabolites may possess equal pharmacological activity or may have modified activity leading to increased or decreased effect. The metabolites produced in many cases are also reported to be toxic compared to the parent drug. Thus, hepatic first pass effect may or may not lead to loss of pharmacological action of drugs. Various formulation approaches for inhibition of hepatic first pass metabolism are employed to enhance the oral bioavailability. There are several approaches to improve problems related to hydrophobic drugs. Among various approaches, nanotechnology-based drug delivery system has potential to overcome the challenges associated with the oral route of administration. Novel drug delivery systems are available in many areas of medicine. The application of these systems in the treatment of hypertension continues to broaden various nano-carriers available in oral drug administration for improving solubility profile, dissolution and consequently bioavailability of hydrophobic antihypertensive drugs. These include its co-administration with another drug (which gets preferentially metabolized), use of prodrugs and promoting drug absorption via lymphatic route (avoiding portal circulation). Novel drug delivery systems e.g. microemulsion, SMEDDS, nanoparticles and liposomes are used widely for avoidance of hepatic first pass effect. This review focuses on oral formulation strategies by which reduction of hepatic first pass metabolism and thus, enhancement of systemic availability of drugs can be achieved. These strategies result in improved bioavailability, reduction in dose and side effects ultimately leading to enhanced patient compliance.

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Biography

Behnaz is currently a graduate student Dubai Pharmacy College, Dubai, His research interest was Drug Delivery, Drug Discovery, Drug Design

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