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Rapid equilibrium dialysis (RED): An In-vitro high-throughput screening technique for plasma protein binding using human and rat plasma

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Determining the extent to which a molecule binds to plasma proteins is a critical phase of drug development because the amount of plasma-bound drug influences compound dosing, efficacy, clearance rate and potential for drug interactions. Determination of the free (%Fu) and bound (%Bound) fractions of a test article in plasma is therefore a critical parameter, which is routinely determined in the process of drug discovery and development. This determination is enabled by equilibrium dialysis, an accepted and standard method for reliable estimation of the non-bound drug fraction in plasma. Although it is the preferred method, equilibrium dialysis has historically been labor-intensive, time-consuming, cost-prohibitive and difficult to automate. A rapid equilibrium dialysis (RED) drug-protein binding assay using LC-MS/MS was developed using a novel technique that resulted in significantly improved assay precision and offers a speed advantage. A panel of compounds covering a range of expected protein binding was tested in plasma of human and rat species. A sensitive and selective method using quadruple tandem mass spectrophotometer interfaced with electro spray ionization was developed for the quantification of un-bound drug in pretreated plasma. The mobile phase used was 0.1 % Formic acid in Acetonitrile: 0.1% Formic acid in Water with gradient HPLC method. The unbound fraction of drugs was detected by mass spectrometer operated in ESI mode. In addition, data for a seven compounds test set was compared to literature values. With the described method, it is possible to screen a relatively large number of compounds for PPB in a drug discovery environment

Exploration of a natural carrier mediated transport system for oral delivery of insulin

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There is greater attention and intensive research on newer drug delivery systems especially with biotherapeutics worldwide today. Among the most important and advantageous drug delivery routes is the peroral route. It offers the greatest potential for more effective therapeutics, but needs to overcome the known natural biological limitations with protective formulations and efficient drug delivery systems.

Insulin administration continues by distressful and intricate injections and a tablet or capsule still remains a long-awaited dream for the mankind. Transgene Biotek is among a few in search of alternate routes and effective delivery mechanisms towards making such dreams come true and has now discovered an explorable new transporter in mammalian intestine, carrying the drug across the intestine to the circulation. The company has developed a novel effective bio-formulation technology employing this proprietary transporter system, forming a targeted nanolattice delivery system.

The concept has been proved with the transcytosis of a monomeric analogue of insulin across the biological barrier by an in vitro enterocyte cell permeability assay using polarized epithelial cells and by performing carrier mediated uptake of the drug in various mammalian cell lines. Our patented proprietary nanolattice formulation technology along with a natural targeting agent is currently being subjected to efficacy studies to monitor reduction in blood glucose levels along with uptake of insulin analogue in the systemic circulation.

Our technology protects the insulin drug from proteolysis in the callous milieu of the intestine, thus enabling it to be administered orally while the targeting agent will ensure efficient gastrointestinal uptake and delivery.