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STRATEGY
There are some very innovative, cutting-edge ideas that Indian pharma leaders are adopting

INTERVIEW
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OPINION

Pharma 4.0: Driving progress with disruptive technologies

Digital and inter-connected data is the foundation for Pharma 4.0. **Lalitha S**, AVP – Strategy, Caliber Technologies, explains more

Pharma 4.0 welcomes a cultural shift by driving processes towards more human-centric workflows that are digitally connected. Pharma companies are embracing this shift by empowering themselves with information systems and making laboratories and factories smart. With these upcoming changes, pharma manufacturing systems must be able to implement corrective actions and instantly respond to demand fluctuations.

With digitalisation at the forefront of Pharma 4.0, the transition to a paperless laboratory is inevitable. The idea is to connect different parts of the value chain and create new levels of adaptivity and transparency for a digitalised system. The concept builds on process analytical technology and Quality by Design (QbD),

Dissolution to permeation to bioavailability: Connecting the dots!

Archana Pokkalath, Research Associate; **Milindkumar Rajput**, Application Scientist; and **Aditya Marfatia**, Director from Electrolab India, enlighten about Dissoflux™, an R&D tool to measure dissolution rate and permeability flux simultaneously, which can aid rank-ordering of formulations based on both solubility and permeability

In case of drug product development, in vitro dissolution and/or release testing is of critical importance, as it facilitates prediction of in vivo product behavior. In case of generics, following the in vitro release testing, in vivo studies need to be performed showing bioequivalence of the test product to the reference product, especially mandatory in case of products containing BCS class II and IV drugs. In order to prove bioequivalence, there should be no significant differences in the bioavailability between the two products. The key factors controlling the in vivo bioavailability are drug dissolution and permeability. A dissolution test facilitates understanding of drug product or formulations in terms of API solubility in the presence of different excipients (in the formulation or dissolution media), variable pH and ionic strength of the dissolution media. However, negligible insights are obtained on how the above mentioned factors affect API permeability.

A latest innovation - Dissoflux™, is an R&D tool to measure dissolution rate and permeability flux simultaneously, which can aid rank-ordering of formulations based on both solubility and permeability. Dissoflux™ consists of a permeation chamber *(Fig 1)*, which holds the permeation sink buffer (PSB). The permeation compartment, also called as acceptor compartment and dissolution media (donor compartment) is separated from a biomimetic membrane mimicking the gastrointestinal tract (For example: PermeaPad® membrane, InnoME and BioWise membrane, BioWise Science LLP). One type of biomimetic membrane involves a membrane substrate used as a solid support for retaining the phospholipid solution. The lipid activated membrane mimics the gastrointestinal lining of the body. An oral dosage form is placed on the dissolution vessel. Drug concentration is monitored in the donor media and in the acceptor compartment to find out the dissolution vs. time profile (a) or drug permeated vs. time profile (c), respectively.

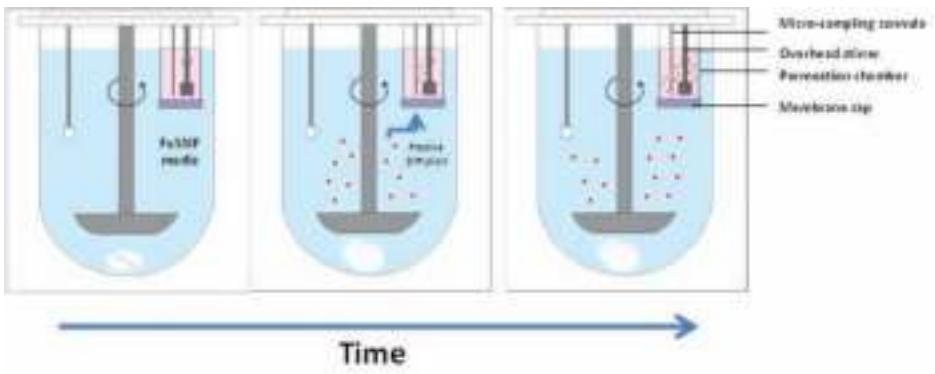

Figure 1: Schematic representation of a dissolution-absorption apparatus (DissofluxTM)

Dissoflux™ can also be used as a preliminary tool for selection of new formulations to be subjected to clinical trials on human subjects. One example is a study that was performed on an approved marketed solid dosage form and a new generic formulation of a BCS class IV drug on dissoflux™. The drug dissolution from the new formulation failed in the f2 factor (similarity factor; f2 value – 42.8) comparison with the innovator product. However, the test formulation and RLD showed a similar permeation trend.

The maximum permeation (ug/cm2 with 90% CI) from the test formulation was within the bioequivalence limit of 80-125% and in parallel to the in vivo behavior. This is an interesting example showcasing the role of permeation of the formulation in bioavailability and can bridge the gap for better predictions for bio results.

By conjunction of the dissolution and permeation aspects of the test formulation, it can be a useful tool to biostatistics scientist to predict the bioavailability of the product. The dissoflux™ test increases the chances of bio success while keeping costs economical and saves time compared to clinical studies. While this tool is a useful predictive instrument for all BCS Classes of drugs that are passively diffused, it is especially useful for BCS class 2 and 4 drugs.

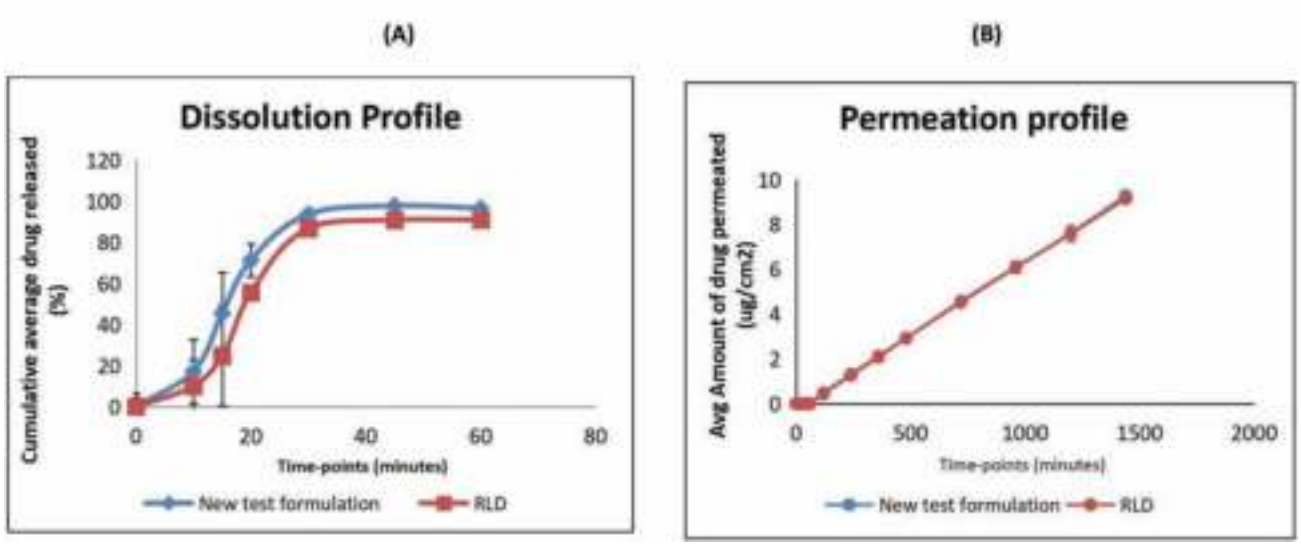

Figure 2: From the dissoflux™ study, the drug concentration is monitored in the donor media and in the acceptor compartment to find out the dissolution vs. time profile (A) or drug permeated vs. time profile (B), respectively

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