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Round Table

The several facets of drug dissolution

Interview

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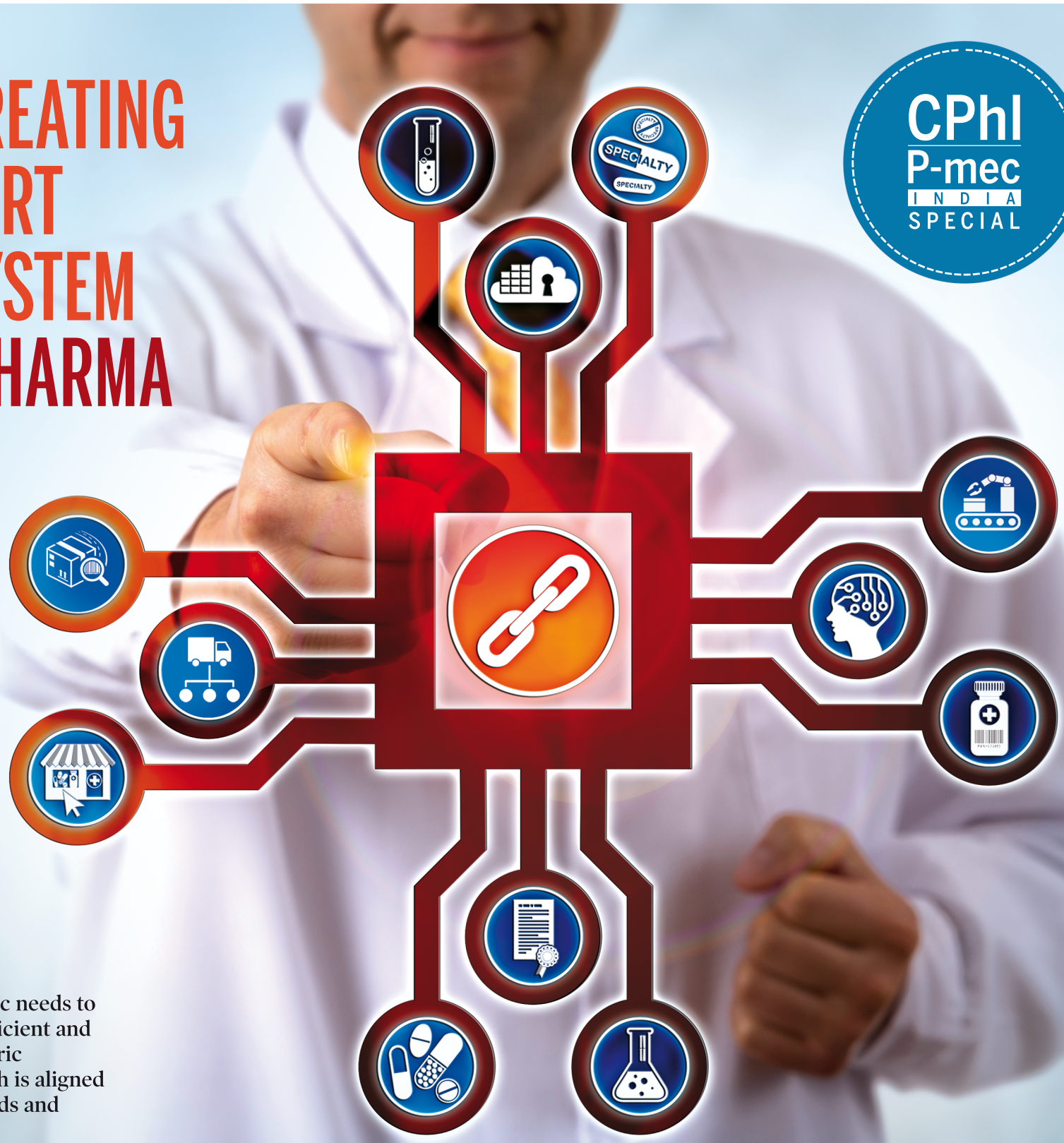
CO-CREATING A SMART ECOSYSTEM FOR PHARMA



CPhI P-mec INDIA SPECIAL

India Pharma Inc needs to build a more efficient and innovation-centric ecosystem which is aligned with global trends and requirements

Transition from manual to automated dissolution sampling: Impact of rinsing

Darshana Kamble, EFFORT Fellow, Electrolab, **Dr Namita Varde**, Application Scientist, Electrolab and **Aditya Marfatia**, Director, Electrolab discuss the nuances of automated sampling, critical parameters to be considered and expand on the usage of different rinsing cycles depending on the application

Dissolution testing plays a critical role throughout the product development cycle right from early formulation development up to quality control. During formulation development, the dissolution profile of all formulations are evaluated and f1, f2 values are compared. However, in quality control, mostly single or two-point dissolutions are conducted to accelerate batch release. During earlier times, manual sampling was the most commonly practiced form of sampling. It is typically performed with the help of syringes or pipettes, where samples are withdrawn directly from the test vessel. Manual sampling is very technique dependent that can result in analyst-to-analyst variability, reproducibility concerns, etc. The pharmacopoeial sampling zone can be either missed or be variable for each time-point resulting in erroneous results.

Automation in dissolution testing is well established. All steps such as test preparation, sample introduction, sampling and cleaning can be automated. Automated sampling facilitates in maintaining the pharmacopoeial sampling zone for every time-point. Automated sampling is a useful alternative to manual sampling, especially if the test includes multiple time-points. In addition, sample filtration can be performed using in line filters, which minimises human intervention. Overall, automated sampling increases accuracy by reducing variability that occurs during manual sampling and enhances compliance to time points, sampling zone and sample volume.

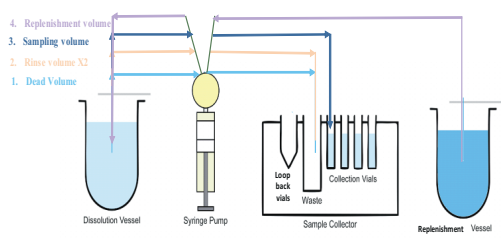
Darshana Kamble, EFFORT Fellow, Electrolab

Dr Namita Varde, Application Scientist, Electrolab

Aditya Marfatia, Director, Electrolab

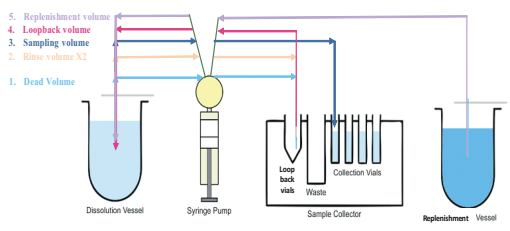
Automation in sampling can be achieved by tube attachments from the test vessel or by robotic devices. Most commonly, samples are collected with the use of a syringe pump, which can then be analysed online via UV/HPLC or offline post-test. The USP guidelines state that manual and automated procedures should be compared to evaluate the interchangeability of the procedures. In addition, it is a requirement that the difference in mean values for dissolution results between the manual and automated tests be <10 per cent for time-points with <85

1. Rinse by Purge



Sr No.	Steps	Collected from	Dispensed to
1	Dead volume	Dissolution vessel	Waste
2	Rinse volume	Dissolution vessel	Waste
3	Sampling	Dissolution vessel	Collection vials
4	Replenishment	Replenishment vessel	Dissolution vessel

2. Rinse by LoopBack



Sr No.	Steps	Collected from	Dispensed to
1	Dead volume	Dissolution vessel	Loopback vial
2	Rinse volume	Dissolution vessel	Loopback vial
3	Sampling	Dissolution vessel	Collection vials
4	Loopback	Loopback vial	Dissolution vessel
5	Replenishment	Replenishment vessel	Dissolution vessel

per cent dissolved and be <5 per cent for time-points with >85 per cent dissolved.

There are several considerations which have to be taken into account while performing automated sampling. Sampling volume has to be stated considering the dead volumes of the tubings. The in line filter type, size and pore size has to be optimised to prevent any pressure buildup during sampling. Rinsing cycles need to be optimised such that no carryover effects are observed in the following time-points. Designing an optimum rinsing cycle is important to match the automatic sampling dissolution profile with the manual sampling dissolution profile as required by USP. There are several advanced rinsing cycles, which can help achieve overlapping profiles when using automatic sampling.

Rinse by Purge

In this cycle, both dead volume and rinse volume is dispensed to waste, which results in loss of drug as well. This cycle is recommended for high label claim drug products.

Rinse by LoopBack

In this cycle, both dead volume and rinse volume is dispensed to the loop back vial, which avoids drug loss. This cycle is recommended for low label claim drug products.

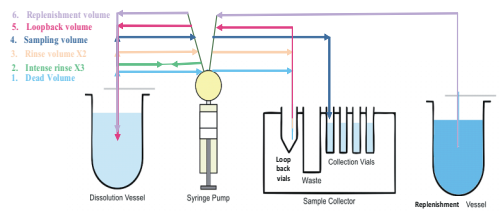
Rinse by IntenseRinse

In this cycle, to better mimic the real-time concentration in the dissolution vessel, i.e. for better tube saturation, a small volume is continuously draw-purged from the dissolution vessel before sampling. This cycle is recommended for low label claim drug products and for API or excipients that are known to adsorb on the tubings.

Rinse by AirPurge

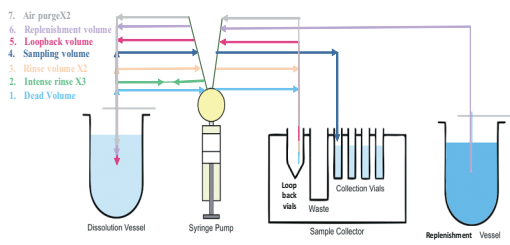
In this cycle, to better mimic manual dissolution sampling, the tubings are emptied out in the last step of sampling. This cycle is recommended for drug products requiring small medium volumes.

3. Rinse by IntenseRinse

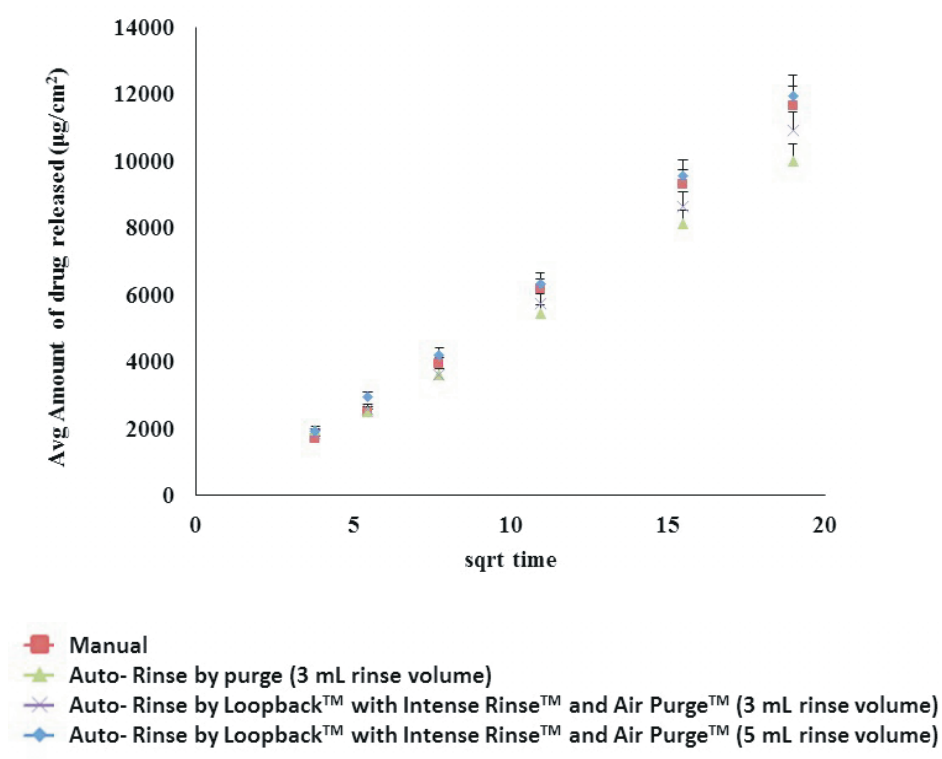


Sr No.	Steps	Collected from	Dispensed to
1	Dead volume	Dissolution vessel	Loopback vial
2	Intense rinse	Dissolution vessel	Dissolution vessel
3	Rinse volume	Dissolution vessel	Loopback vial
4	Sampling	Dissolution vessel	Collection vials
5	Loopback	Loopback vial	Dissolution vessel
6	Replenishment	Replenishment vessel	Dissolution vessel

4. Rinse by AirPurge



Sr No.	Steps	Collected from	Dispensed to
1	Dead volume	Dissolution vessel	Loopback vial
2	Intense rinse	Dissolution vessel	Dissolution vessel
3	Rinse volume	Dissolution vessel	Loopback vial
4	Sampling	Dissolution vessel	Collection vials
5	Loopback	Loopback vial	Dissolution vessel
6	Replenishment	Replenishment vessel	Dissolution vessel
7	Air purge	Sample collector	Dissolution vessel



Manual to Automatic sampling transition for a BCS Class I containing drug product

The impact of rinse volume (3 and 5 mL) and LoopBack, IntenseRinse and AirPurge cycles was evaluated by investigating the differences in the release rate of BCS class I drug Lidocaine hydrochloride from water based topical marketed gel LOX 2 per cent. The release study was performed using an Immersion cell (Enhancer cell) apparatus. An immersion cell of 2 cm2 orifice was used. The average amount of gel filled in each cell was 1.6 g (-32 mg API). A nitrocellulose membrane of 0.45 µ and 25 mm diameter was used. 200 mL of acetate buffer, pH 4.5 was used at the medium. The test was performed at 32°C for six hours. It was observed that the profile obtained with LoopBack, IntenseRinse and AirPurge (rinse volume of 5 mL) cycle did not demonstrate statistically significant difference when compared with the manual test profile.

References

1. Chapter <711>Dissolution of USP 41

2. Chapter <1092>The Dissolution Procedure: Development and Validation