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Topics for the Next Issue

The August 2026 issue will include a *Stimuli* article for operation of USP apparatus 4; research articles on alpha-lipoic acid dietary supplements, tofacitinib citrate tablets, bentonite-based suppository, and baclofen tablets, as well as the Q and A feature.

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USP Guideline on Procedures for Mechanical Performance Qualification for USP Apparatus 3 – Reciprocating Cylinder

Vivian A. Gray[1], Bryan Crist[1], Brandon Maris[1], Harsh S. Shah[1], Kimberly D. Dunn[1], Martin Coffey[1], Pascal St-Laurent[1], Mark R. Liddell[2], and Margareth R. C. Marques[2]

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ABSTRACT

This USP guideline represents the current best practices for determining mechanical qualification performance for USP apparatus 3, described in Dissolution <711>. The guideline covers the performance qualification topics of environment, benchtop levelness, assembly, apparatus conformance, alignments, drive system and transmission, temperature control, component certification, periodic preventative maintenance, physical parameter measurement, and operational checks. This guideline is intended to provide information that aids the dissolution laboratory in establishing appropriate standard operating procedures to verify compliance with compendial requirements and ensure valid dissolution and drug release testing results.

USP welcomes proposals for a drug product that could be used as a final performance qualification to assess the overall suitability of the equipment.

INTRODUCTION

This guideline outlines best practices for the mechanical performance qualification of the USP apparatus 3 - reciprocating cylinder. The best practices have been developed on the basis of experience gained by the USP laboratory and with suggestions from the Performance Verification Testing Standard Expert Panel under the guidance of the USP General Chapters—Dosage Forms Expert Committee. While not a standard requiring rigid compliance, this guideline is intended to provide information that aids the dissolution laboratory in establishing appropriate standard operating procedures to verify compliance with compendial requirements and ensure valid dissolution and drug release testing results.

This version of the document represents a continuing effort to provide detailed information describing the procedures that, if used, will ensure a properly qualified dissolution test assembly. As new information relevant to that goal becomes available, this document may be revised by the USP.

Analytical instrumental qualification (AIQ), which includes installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ), is widely accepted. For dissolution assemblies, the mechanical qualification steps outlined in this guide should satisfy the OQ and parts of Analytical Instrument Qualification <1058>.

The USP Chlorpheniramine Maleate Extended Release Tablets RS used in the performance verification tests (PVTs) for USP Apparatus 3 was discontinued effective February 2012. Because there is no replacement USP PVT for the reciprocating cylinder apparatus at this time, a mechanical means of apparatus qualification may be used to demonstrate that the apparatus is suitable for its intended use.

USP is seeking proposals for drug products that could be used in the PVT of USP Apparatus 3. These drug products should have a modified-release mechanism compatible with the functioning of USP Apparatus 3—for example, not disintegrating completely in the first row of the apparatus and exhibiting a release rate that allows for two or more sampling time points over a reasonable test length. Please address any suggestions to Margareth R. C. Marques at mrm@usp.org.

DEFINITIONS

Agitation Element

An *agitation element* is the shaft for attaching the reciprocating cylinder containing the dosage form. The up-and-down motion provides agitation to promote the movement of the dissolution medium through the reciprocating cylinder relative to the dosage unit under test.

Apparatus

An *apparatus* is the basic unit for the in vitro performance testing of dosage units. The apparatus consists of a container (vessel) for the dosage unit and the dissolution medium, a device for promoting motion of the dissolution medium (agitation element), temperature control, and a support to hold the vessel and reciprocating element in a fixed orientation. Typically, 6–8 apparatuses are grouped in a dissolution test assembly.

Assembly

An *assembly* is a combination of multiple positions within the apparatus that provide temperature control; controlled sinusoidal motion of the reciprocating shafts; and the capability for simultaneous starting, stopping, and movement of the reciprocating cylinders from row to row. The time required for the reciprocating shafts for the upward stroke is equal to the time required for the downward stroke, and the change in stroke direction is a smooth transition, rather than an abrupt reversal of motion.

Base Plate

The *base plate* is the structural element or frame of the test assembly that fixes and provides support for the removable vessel plates during testing. Vessel support plates may be permanently incorporated into the base or removable from the base.

Calibration

Calibration is a process, performed under a set of specified and controlled measurement conditions, that establishes a relationship between the indication or output of the measurement device (with measurement uncertainties) and accepted measurement standards (with their corresponding indications and associated measurement uncertainties; see Dissolution <711>).

Dissolution System

The *dissolution system* includes USP Apparatus 3, which may be connected to a sampling and filter unit and may include on-line instrumentation such as a UV–Vis spectrophotometer or an HPLC system.

Drive Unit Plate

The *drive unit plate* is a support structure that holds the drive mechanism for the reciprocating elements. The moving parts of the drive unit are protected from contamination by a cover that also shields against operator injury. The removable drive unit cover is not typically considered a suitable surface to determine the levelness of the drive unit plate.

Position

The *position* is the location within the USP Apparatus 3 test assembly where a particular vessel and reciprocating cylinder are situated (e.g., row 1, vessel 1).

Run

A *run* is common terminology for the dissolution sample aliquot preparation procedure. As stated in <711>, Interpretation, the smallest sample set tested comprises six dosage units. A run may include multiple sampling intervals but is concluded by the withdrawal of the sample aliquots (with filtration) at the final specified time point.

Vessel Support Plates

Vessel support plates should hold vessels in place during the test. Vessel plates may be removable but should be returned to their original location if removed and replaced.

PERFORMANCE QUALIFICATION

Environment

Benchtops are used to support dissolution equipment. A suitable benchtop must be level and sturdy and provide a high inertial mass to limit vibration. Disturbances, such

as the placement of containers holding large volumes of solution, may produce transient vibrations but should not affect the levelness of the surface.

Benchtop Levelness

A digital or spirit level should be used to measure the inclination of the benchtop in two orthogonal directions. Benchtop surface inclination should be no more than 1°. The influence of benchtop surface inclination on the dissolution assembly can be compensated for by leveling devices (see Apparatus Conformance and Vessel Plates sections below).

Assembly

All vessels and reciprocating cylinder components should meet USP specifications and be dedicated to each test assembly for all dissolution runs. For ease of identification and recordkeeping, apparatus positions on the vessel support plate of the dissolution test assembly should be identified systematically.

Apparatus Conformance

Vessel and Reciprocating Cylinder Components

Vessels and reciprocating cylinder components conform to the dimensional requirements of <711>, as shown in Figure 1. Use a Vernier caliper, depth gauge, or other suitable measurement devices to confirm that the measurements meet the specifications. The vessels' inner surfaces must be clean, without significant etching or scratches.

Vessel Plates

A spirit level may be used on the frame supporting the removable vessel plates. The inclination is not more than 0.5° in each of two orthogonal directions. Figure 2 shows that a reading closer to 0.0° can be achieved. Most base plate designs allow adjustment of levelness, if necessary, usually by rotating adjusting screws on the feet of the support and frame assembly. If the apparatus is not level after maximum adjustment, it should be moved to a more level area. The strain on the test assembly structure due to the mass of the filled water bath and vessels should be taken into account. Thus, the levelness of the vessel support frame should be confirmed with the water bath filled. The condition of the removable vessel support plate(s) should be visually evaluated and confirmed to be uniform, even, and free of distortion or deformation. The removable vessel support plate(s) should resist deformation when under load by filled vessels and should remain level. The vessel support plate(s) should not be corroded to a point where vessel perpendicularity may be jeopardized.

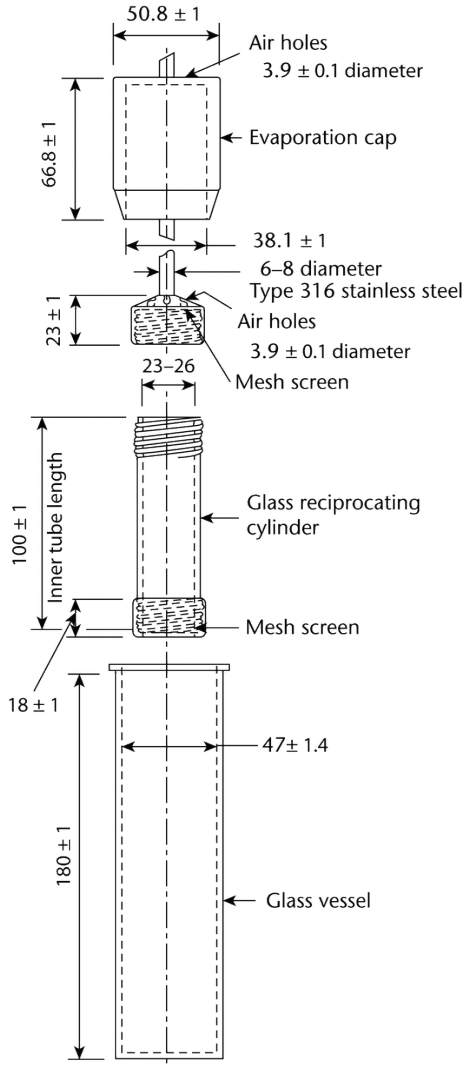

Figure 1. Apparatus 3 - reciprocating cylinder. All measurements are expressed in millimeters unless otherwise noted.

Alignments

Shaft Verticality

Use a digital protractor (level) to check the verticality of the reciprocating shafts. Measure the verticality for each shaft in two vertical planes at 90.0° angles to each other (see Fig. 3). The deviation should be no more than 0.5° from 90.0° for these measurements.

Vessel Verticality

With the vessels in their run position, place a machinist square into the vessel, taking care not to scratch the surface, and place a digital level or spirit level on the perpendicular surface to determine vessel verticality (Fig. 4). Note that excess pressure on the wall of the vessel may misalign the vessel, causing inaccurate

Figure 2. Electronic level on the USP apparatus 3 vessel plate.

measurement. Measure the verticality for each vessel in two positions oriented at 90.0° around the vessel axis. The ideal reading obtained on a horizontal surface of the machinist square is 0.0°. The deviation should be no more than 0.5° from 0.0° for this measurement. No part of the assembly, including its surrounding environment, should contribute motion, agitation, or vibration other than that caused by the smooth, vertically reciprocating shaft.

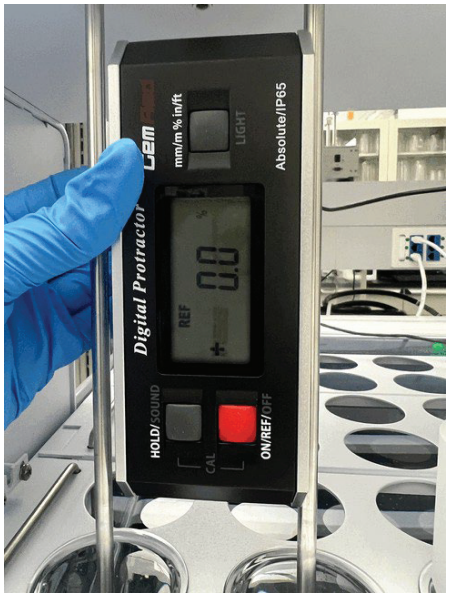

Figure 3. Electronic level to determine shaft verticality of apparatus 3.

Drive System and Transmission

Reciprocation Rate

Measure the reciprocation rate of all shafts using a calibrated timer or digital tachometer (see Fig. 5). The reciprocation rate should be evaluated at both 10 and 50 dips per minute (dpm) or in a range to cover the methods used on the instrument. The calibration range should be stated on the calibration label affixed to the instrument. All measured speeds should be within ± 5% of the set rate.

Temperature Control

Place vessels containing 250 mL of water in each position of the system. With the temperature control set to achieve 37.0° in the vessels and the shafts and evaporation caps lowered into position, measure and document the temperature of the water in each vessel using a calibrated thermometer once they have had time to equilibrate. After equilibration, the medium temperature measured in all vessels should agree within a range of 0.5° and within ± 0.5° of the set temperature.

QUALIFICATION PROCEDURES

Relying on an enhanced mechanical qualification approach, in the absence of a PVT for the USP apparatus 3 - reciprocating cylinder, these mechanical steps should be performed periodically at a frequency determined by an internal risk assessment to maintain the apparatus in a qualified state.

The following steps should be implemented to ensure a current state of qualification of the reciprocating cylinder apparatus: certification of components, documentation of scheduled preventative maintenance, mechanical qualification parameter measurement, and operational checks to be performed at the time of testing.

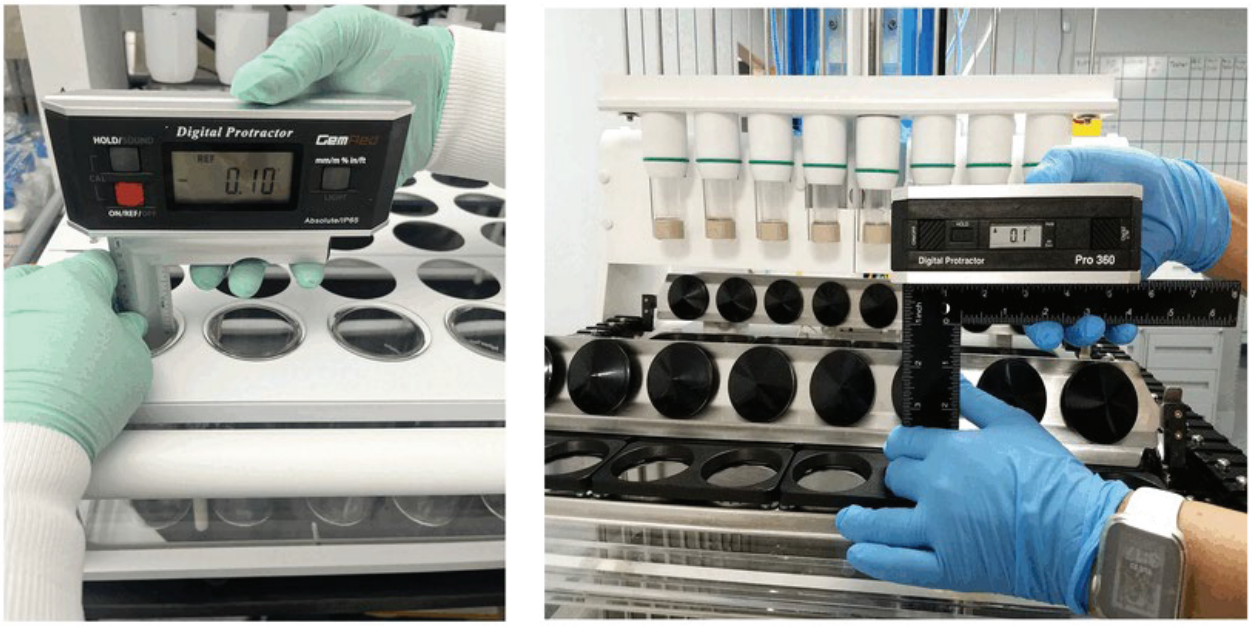

Figure 4. Measurement of apparatus 3 vessel verticality.

Figure 5. Digital measurement of the reciprocation rate. (Printed with permission of Logan Instruments).

Component Certification

Documentation should be established for each reciprocating cylinder apparatus component to demonstrate that it meets the specifications and tolerances according to <711> (see Fig. 1 and Table 1). Certificates of conformance (CoCs) with actual measurements and acceptance criteria may be obtainable from dissolution apparatus manufacturers. If certificates are unavailable, conformance measurements may be conducted by the end user and documented. Regarding screens used for analysis, screen sizes are described in standards such as ASTM E11-09 and ISO 3310-1:2016 (*1*, *2*).

(NOTE—Specialized tools may be required to measure screen size and the internal diameter of the reciprocating cylinder.)

Table 1. Specifications and Tolerances for Reciprocating Cylinder Apparatus Component

Component	Specification and Tolerance		Material of Construction
Shaft	Diameter: 7 ± 1 mm	—	Inert (e.g., SS316[a])
Vessels	Height: 180 ± 1 mm	Inner diameter: 47 ± 1.4 mm	Inert (e.g., glass)
Reciprocating cylinders	Height: 100 ± 1 mm	Inner diameter: 25 ± 2.0 mm	Inert (e.g., glass)
Upper cap	Height: 23 ± 1 mm	Air hole diameter: 3.9 ± 0.1 mm	Inert (e.g., polypropylene)
Lower cap	Height: 18 ± 1 mm	—	Inert (e.g., polypropylene)
Evaporation cap	Height: 66.8 ± 1 mm Outer diameter: 50.8 ± 1 mm	Inner diameter: 38.1 ± 1 mm Air hole diameter: 3.9 ± 0.1 mm	Inert
Screens	As defined in the specific method or monograph	If not specified, use dimensions from ASTM or ISO standards	Inert (e.g., SS316 or polypropylene)

[a]*SS316 = Stainless steel grade 316.*

Preventive Maintenance

The apparatus must undergo periodic maintenance (PM) to ensure it is in proper condition. The PM intervals are to be determined by the quality system and usually coincide with the periodic qualification of the apparatus. Manufacturer recommendations for PM—including cleaning, lubrication, and replacement of parts—should be followed. (NOTE—The apparatus should be disconnected from the power source before doing any maintenance, and these steps should only be performed by qualified or trained maintenance personnel.)

- Inspect the condition of vessels, cylinders, caps, and agitator shaft O-rings.
- Ensure that vessel evaporation covers do not disrupt the centering of the glass vessels.
- Clean and lubricate the horizontal guides and agitator shafts with the recommended lubricant, as directed by the manufacturer. Evaluate internal components by unplugging and removing the outer cover to examine:
  - Belt for damage or wear
  - Belt tension specific to the manufacturer's recommended specification
  - Lubricate arms and mechanical linkages with the recommended lubricant as directed by the manufacturer
- Check communication and control cables, as well as power cords, which should not show signs of wear, damage, or corrosion.
- Check the bath heater, circulator, and tubing for blockage, damage, or algae growth; replace as needed.

Physical Parameter Measurement

The following operating parameters must be periodically measured to ensure the apparatus is operating in a qualified state:

- Vessel temperature: 37.0 ± 0.5 °C
- Dip rate: ± 5% of set speed
- Stroke distance: 10.0 ± 0.1 cm
- Bottom screen: Per method, dimensions subject to ASTM 3 or ISO 4
- Top screen: Per method (optional), dimensions subject to ASTM 3 or ISO 4
- Time points: ± 2% of the specified time to start sampling

Stroke Distance

Depending on the apparatus design, the assembly manufacturer may provide a calibrated caliper to be mounted onto the dipping manifold or shaft to measure the stroke distance of the reciprocating apparatus, as shown in Figure 6. For instruments without a measurement tool, apply tape to the vertical shaft assembly and place a mark on the tape as it reciprocates using a fine-tip marker. The tape may be temporarily left in place and measured or removed and recorded in a logbook. After placing the mark on the tape, measure the length of the mark with a calibrated caliper, as shown in Figures 7 and 8. Alternatively, other appropriate digital tools may be used.

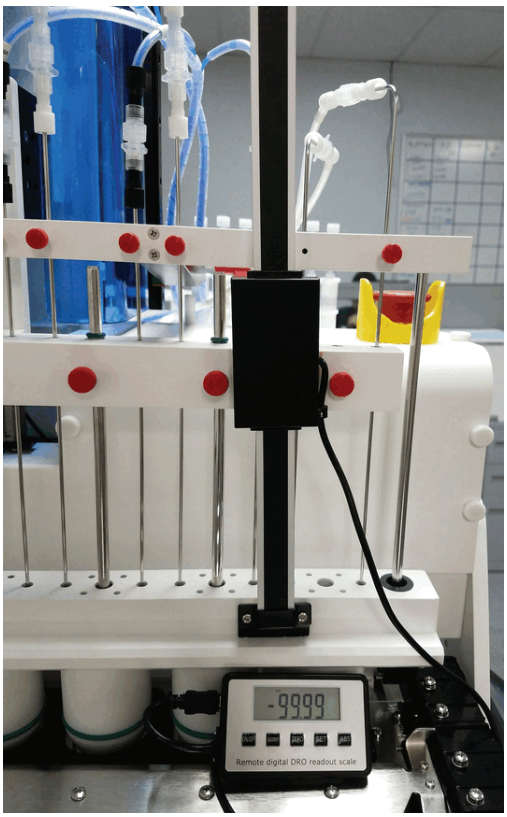

Figure 6. Digital caliper for measuring stroke distance. (Printed with permission of Logan Instruments).

Operational Checks

Before each run with USP apparatus 3, the analyst should perform and document the following checks on the apparatus to ensure that it is suitable for its intended purpose:

1. Reciprocating cylinders' glass surfaces are free from residue, scratches, and cracks.
2. Screens are the appropriate dimension required by the method and are not damaged, frayed, misshapen, or corroded.

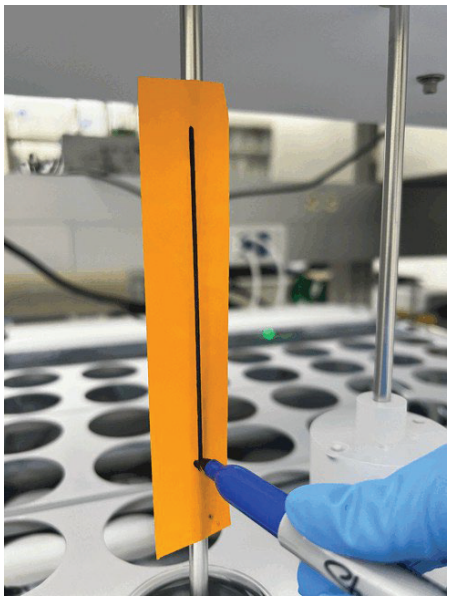

Figure 7. Recording stroke distance with fine-tip marker.

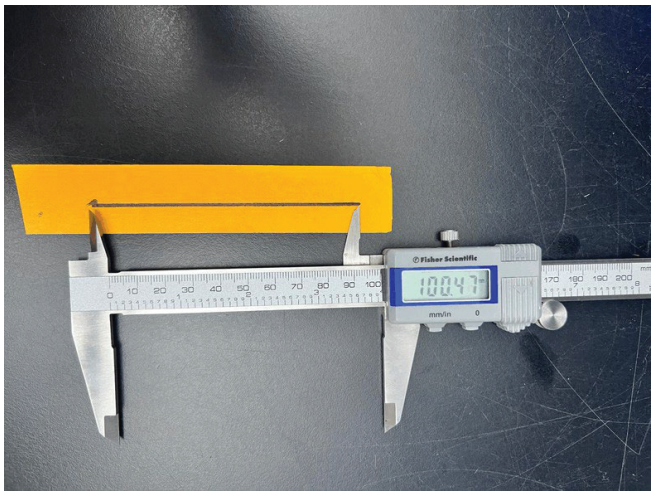

Figure 8. Measuring stroke distance with a calibrated caliper.

3. Vessels are clean and free from residue, scratches, and cracks.
4. Vessels remain stationary during the test.
5. Upper and lower caps are clean and free from residue.
6. Vessel temperature is maintained at 37.0 ± 0.5 °C (beginning and end of run).
7. Evaporation covers are properly fitted to allow shafts to reciprocate freely without moving the evaporation cover or pushing the vessel off center while the cylinder is reciprocating. Proper evaporation control should be maintained for all vessels and positions.

Periodicity and Frequency

USP recommends the following periodicity associated with mechanical calibration:

1. Scheduled mechanical qualification of the apparatus should be performed at a frequency determined by the quality system or after repair, movement, or relocation of the apparatus.
2. Once the apparatus meets the acceptance criteria included in <711>, the instrument is considered qualified. (NOTE—There is no current USP PVT for apparatus 3.) Prior to each test, the analyst should perform and document the operational checks outlined above.

APPENDIX

Equipment Used in Mechanical Calibration

Caliper

A *caliper* measures the distance between two opposing points or surfaces. The trueness and precision of caliper measurements can be checked using gauge blocks. Gauge blocks are standardized materials that represent specific distances and are used as reference standards for calibrating measuring tools.

Digital Protractor or Digital Level

A *digital protractor or digital level* is used to measure the inclination of an object. A digital protractor indicates degrees of inclination by electronic means and provides a more precise measurement compared with spirit or bubble levels.

Stopwatch

A *stopwatch* is a calibrated, traceable timing device used to measure reciprocation rate or dips per minute (dpm).

Thermometer

A *thermometer* is a calibrated device used to measure the temperature of the water bath and dissolution medium in the vessels.

DISCLAIMER

Certain commercial equipment, instruments, vendors, or materials may be identified in this article to specify adequately the experimental procedure. Such

identification does not imply approval, endorsement, or certification by USP of a particular brand or product, nor does it imply that the equipment, instrument, vendor, or material is necessarily the best available for the purpose or that any other brand or product was judged to be unsatisfactory or inadequate.

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2. ISO 3310-1:2016: Test Sieves—Technical Requirements and Testing—Part 1: Test Sieves of Metal Wire Cloth. The International Organization for Standardization; 2016.

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The Effect of Lyophilization on Solubility and Dissolution Enhancement of Furosemide: In Vitro Assessment and Kinetic Modeling

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ABSTRACT

Background: Furosemide, a BCS class IV diuretic, demonstrates inadequate water solubility and restricted intestinal permeability, leading to suboptimal oral bioavailability. Enhancing its dissolution is essential for improving therapeutic efficacy. This study assessed the effect of lyophilization on the in-vitro solubility profile of furosemide relative to the pure drug, Lasix (reference product), and a commercially available generic formulation. **Methods:** A lyophilized formulation of furosemide was developed using sucrose as a cryoprotectant and subjected to freeze-drying under regulated circumstances. Dissolution testing was conducted with a USP type 2 paddle apparatus in 0.1 N HCl, and drug concentrations were measured via UV-Vis spectrophotometry (λmax = 229 nm). Dissolution kinetics were analyzed using the Korsmeyer–Peppas model, and the dissolution profiles were evaluated with the difference factor (f_1). **Results:** The lyophilized formulation exhibited markedly superior solubility relative to the other formulations. Kinetic release adhered to a Fickian diffusion mechanism (n = 0.051), having enhanced porosity and partial amorphization. Conversely, the pure drug demonstrated a more gradual release profile (n = 0.667). The f_1 value between Lasix and the lyophilized formulation was above 160, signifying considerable dissimilarity. **Conclusion:** Lyophilization significantly enhanced the solubility of furosemide by altering its physicochemical properties. Nonetheless, owing to the significant disparities in dissolution patterns, further bioequivalence and pharmacokinetic investigations are necessary to validate clinical interchangeability.

KEYWORDS: Furosemide, lyophilization, dissolution enhancement, solubility enhancement, dissolution

INTRODUCTION

Furosemide is a potent loop diuretic frequently prescribed for the management of edema associated with congestive heart failure, liver cirrhosis, and renal dysfunction, and for controlling hypertension. Despite its clinical utility, furosemide exhibits low aqueous solubility and poor intestinal permeability, categorizing it under Biopharmaceutics Classification System (BCS) class IV. These physicochemical constraints lead to inconsistent and significantly low oral bioavailability, with a tendency to display considerable inter- and intrasubject variability (*1*). Numerous formulation strategies have been explored to overcome solubility barriers, including solid dispersions, salt formation, cyclodextrin inclusion complexes, self-emulsifying drug delivery systems, and nanosuspensions (*2*–*7*). However, each method carries specific limitations in terms of scalability, stability, and reproducibility.

Lyophilization (freeze-drying) is gaining traction as a versatile technique for enhancing the dissolution of poorly soluble drugs (*8*). It transforms the active pharmaceutical ingredient (API) into an amorphous, porous structure with significantly higher surface area, thereby facilitating faster wetting and dissolution upon contact with gastrointestinal fluids (*9*). Previous studies have demonstrated the ability of lyophilization to improve the dissolution rate and bioavailability of BCS Class IV drugs (*10*). Despite these advances, limited literature

*Corresponding author

exists on the application of lyophilization to furosemide, especially in comparison with commercial reference and generic formulations.

This study aimed to examine the impact of lyophilization on the dissolution characteristics of furosemide, a BCS class IV drug, by comparing the dissolution profiles of the lyophilized formulation with those of the pure drug, the reference product (Lasix), and a marketed generic formulation. This study aims to determine if lyophilization could serve as an effective method to enhance the solubility and release properties of furosemide.

METHODS

Materials

Pure furosemide was procured from Pioneer (Iraq). Lasix 40-mg tablets (Sanofi, France; batch 4LU9A; expiration 02/2027) were used as the reference listed drug and purchased from the local market, as well as a generic furosemide tablet formulation (Accord Healthcare, UK; batch 09A246; expiration 09/2026). Sucrose (used as a cryoprotectant) and analytical-grade reagents were sourced from Alpha Chemica (India). All chemicals used were of pharmaceutical or analytical grade.

Tablet Characterization

Commercial tablets were measured for basic physical attributes using a digital caliper. Lasix 40 mg (Sanofi) was a white, round, scored tablet with an average diameter of 8 mm and a thickness of 2 mm. The generic furosemide tablets were also white and round, with an average diameter of 7 mm and a thickness of 2 mm.

Experimental Methods

Preparation of Lyophilized Formulation

A furosemide-sucrose solution was prepared in distilled water containing 10% w/w furosemide and 90% w/w sucrose after freeze-drying. The solution was first homogenized, then pre-frozen at −55 °C. Primary drying was performed using a laboratory freeze dryer (Alpha 1-2 LSCbasic, Germany) under a vacuum of 0.01 mbar at −55 °C for 10 hours, followed by secondary drying at 0 °C to remove residual moisture for 12 hours. The formulations were prepared and stored in 10 mL type I glass vials, sealed with laboratory-grade rubber stoppers and secured with Parafilm. Samples were kept in desiccators at room temperature (approximately 25 °C), protected from light, and tested within 3 days of lyophilization (*11*). The outcome of the process was a lyophilized powder obtained as uniform, white, and porous cakes with no evidence of collapse or shrinkage during processing. No final dosage form was developed at this stage.

Solubility Studies

The inherent aqueous solubility of pure furosemide was determined under standardized conditions to establish a baseline for comparison with formulated products. Excess pure furosemide was introduced to 10 mL of distilled water and incubated at 37 °C with continuous agitation for 72 hours to attain equilibrium. The solubility experiment was performed in triplicate (n = 3). After filtration through 0.45-µm syringe filters, the saturated concentration was measured using UV-Vis spectrophotometry (UV-1800, Shimadzu, Japan) (*12*).

Identification and Calibration

Furosemide was identified by UV-Vis spectroscopy, with a maximum absorbance (λmax) observed at 229 nm in 0.1 N HCl (*13*). A calibration curve was established using standard solutions ranging from 0.1–0.7 µg/mL. The calibration equation was derived by plotting absorbance against concentration, demonstrating linearity with R^2 = 0.998.

In Vitro Dissolution Testing

Dissolution profiles were assessed using the USP apparatus 2 (paddle method; PTWS 120D, Pharma Test, Germany), with 900 mL of (0.1 N HCl) as the dissolution medium. The pH of the medium was verified using a digital pH meter (3510, Jenway, UK). The temperature was maintained at 37 ± 0.5 °C, and the paddle speed was set at 50 rpm. Powdered samples were placed inside a small semi-permeable membrane pouch. The pouch was gently opened at the surface of the dissolution medium to allow uniform and immediate dispersion while preventing floating or adhesion to the vessel walls. For all formulations, the sample amount used in the dissolution test provided an equivalent furosemide dose of 40 mg. This corresponded to 40 mg of raw furosemide, 40 mg furosemide-equivalent from the physical mixture, and 400 mg of lyophilized powder based on a 10% drug loading. Samples were withdrawn at predetermined intervals (0, 5, 10, 15, 30, 45, and 60 minutes), filtered using 0.45-µm polytetrafluoroethylene (PTFE) membrane syringe filters, and analyzed at 229 nm using UV spectrophotometry (*14*).

Data Analysis

Dissolution data were analyzed using DD Solver version 1.0. The goodness of fit was assessed using the maximum correlation coefficient (R^2) and the minimum Akaike Information Criterion (AIC) values. Model-independent comparison between formulations was carried out using the difference factor (f_1). All experiments were performed in triplicate, and the data are expressed as mean ± SD.

Statistical analysis was conducted using one-way ANOVA, with differences considered statistically significant at a p-value less than 0.05 (*15*).

RESULTS

Solubility

The intrinsic saturation solubility of pure furosemide in distilled water at 37 °C was established as 1.9 ± 0.5 µg/mL. This value is in close agreement with previously published data, which reported a solubility of 1.8 ug/mL under similar conditions (*16*). The lyophilized formulation exhibited more than a 10-fold increase in solubility relative to the pure drug.

Dissolution Testing

The cumulative percentage of drug released over time for each formulation is summarized in Table 1 and graphically represented in Figure 1. The lyophilized formulation exhibited a markedly enhanced dissolution profile compared to all other formulations. A rapid initial release was observed, with approximately 86% drug release within the first 5 minutes, followed by sustained release reaching nearly 90% at 60 minutes.

Table 1. Cumulative Drug Release (%) of Different Furosemide Formulations at Various Time Intervals

Time (min)	Pure furosemide	Lasix	Generic	Lyophilized
0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
5	1.6 ± 0.5	24.6 ± 2.1	22.3 ± 1.8	86.7 ± 3.5
10	7.3 ± 0.9	31.5 ± 2.4	29.7 ± 2.2	71.6 ± 3.1
15	9.6 ± 1.1	34.9 ± 2.0	32.2 ± 2.3	79.3 ± 2.8
20	11.3 ± 1.4	39.5 ± 2.6	34.9 ± 2.7	83.5 ± 3.6
25	12.1 ± 1.2	44.2 ± 2.8	34.8 ± 2.4	80.6 ± 3.0
30	15.4 ± 1.7	40.7 ± 2.2	36.1 ± 2.6	86.9 ± 4.1
35	16.7 ± 1.5	42.0 ± 2.5	39.3 ± 2.1	87.7 ± 3.7
40	18.8 ± 1.9	46.3 ± 3.0	47.8 ± 3.4	88.5 ± 4.2
45	20.0 ± 2.0	39.6 ± 2.7	48.7 ± 3.1	88.8 ± 3.9
50	20.5 ± 1.8	44.1 ± 2.9	51.6 ± 3.6	87.5 ± 4.0
55	21.7 ± 2.2	46.4 ± 3.1	54.0 ± 3.8	89.1 ± 4.3
60	21.1 ± 1.9	53.3 ± 3.5	52.2 ± 3.2	88.5 ± 3.8

Values are expressed as mean ± SD (n = 3).

In contrast, the pure drug showed a significantly slower release profile, not exceeding 22% at 60 minutes. The reference product (Lasix) and the generic formulation demonstrated moderate release rates, with cumulative releases of approximately 53% and 52%, respectively, at 60 minutes.

Kinetic Modeling

The dissolution data of the four tested formulations were analyzed using DD Solver, applying the Korsmeyer–Peppas model to evaluate the release kinetics (*15*, *17*). The selection of the model was guided by its superior goodness-of-fit parameters, as indicated by the highest R^2 and lowest AIC values when compared to alternative models, including zero-order, first-order, and Higuchi models.

The values of the release exponent (n), kinetic constant (k), R^2, and AIC for each formulation are summarized in Table 2. The Korsmeyer–Peppas model consistently exhibited the lowest AIC values, confirming its superiority over zero-order, first-order, and Higuchi models in describing the release kinetics of all formulations. The lyophilized formulation exhibited the lowest n-value (0.051), consistent with a predominantly Fickian diffusion release pattern. In contrast, pure furosemide (n = 0.667) showed a non-Fickian release mechanism involving both diffusion and matrix relaxation. The reference product (Lasix) and the generic formulation also demonstrated Fickian diffusion patterns but with slower release rates.

Table 2. Korsmeyer–Peppas Kinetic Model Parameters for Furosemide Formulations

Formulation	n-value	k (min^{-n})	R^2	AIC
Pure furosemide	0.667	1.5	0.9748	40.2
Lasix	0.243	18.05	0.9533	63.94
Generic furosemide	0.378	11.27	0.9704	60.77
Lyophilized formulation	0.051	71.725	0.9715	72.75

n = release exponent; k = kinetic constant (min^{-n}); R^2 = correlation coefficient; AIC = Akaike Information Criterion.

Figure 2 further illustrates the observed versus predicted dissolution profiles, demonstrating the close agreement of the model with the experimental data for Lasix, the generic formulation, pure furosemide, and the lyophilized product.

Difference Factor (f_1) Analysis

To further evaluate the similarity between the lyophilized formulation and marketed products, f_1 was calculated based on model-independent comparison criteria recommended by the U.S. Food and Drug Administration (FDA) (*18*). An f_1 value between 0 and 15 indicates that the two dissolution profiles are similar. In the present study, only the generic formulation (f_1 = 8.45) met this criterion, demonstrating statistical similarity to the reference product (Lasix). By contrast, the pure drug (f_1 = 26.13) and the lyophilized formulation (f_1 = 162.23) exceeded the threshold, indicating substantial dissimilar-

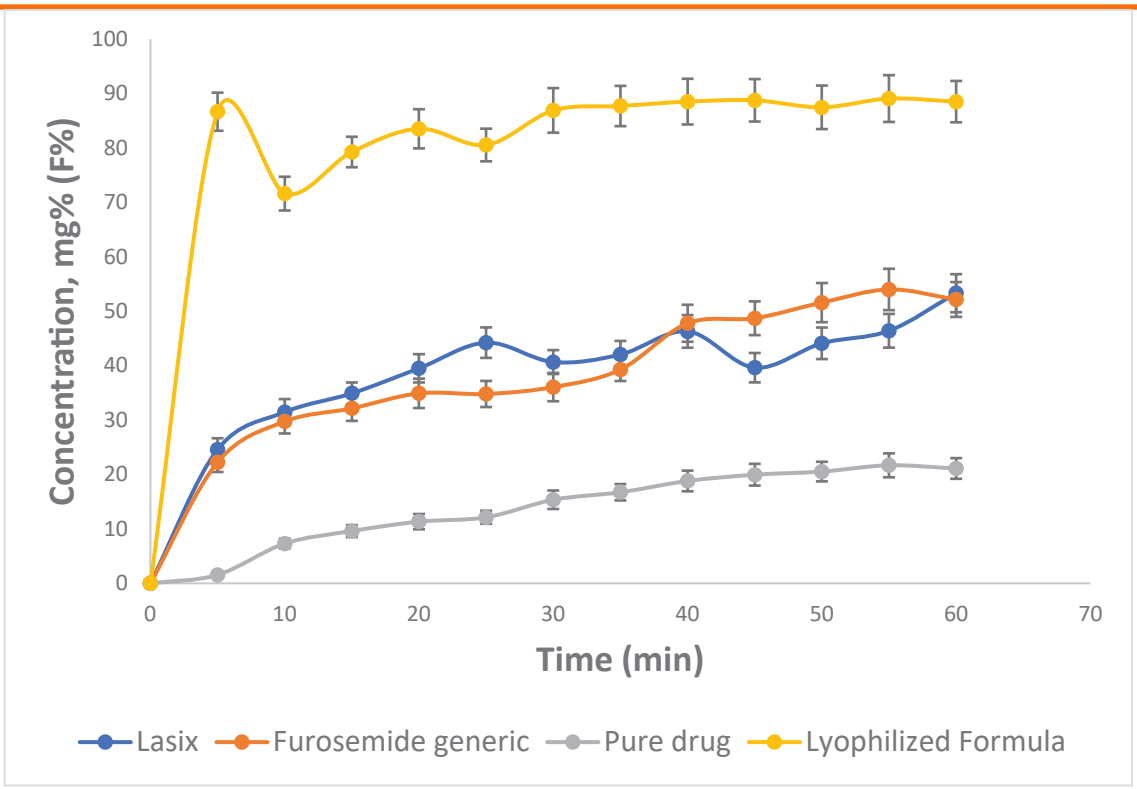

Figure 1. Dissolution profiles of furosemide formulations over 60 minutes in 0.1 N HCl.

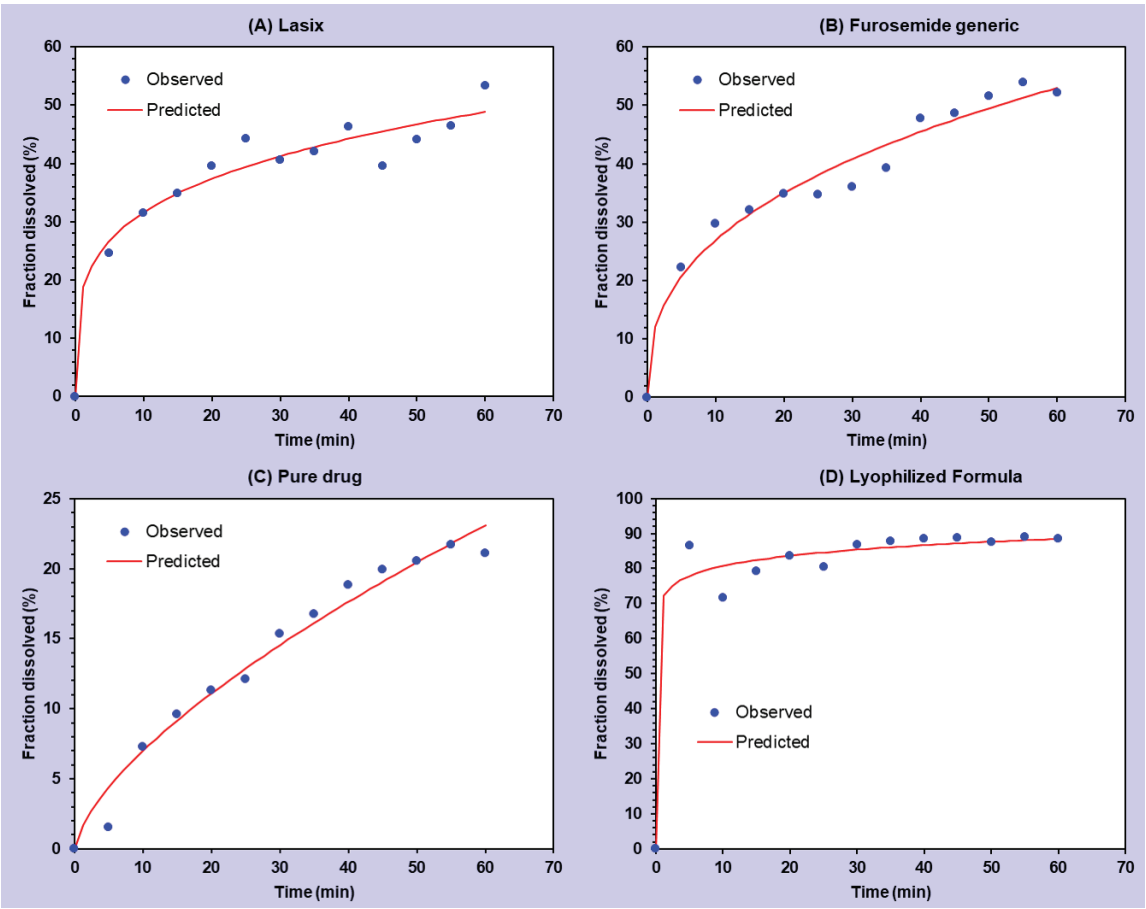

*Figure 2. Observed (dots) and predicted (lines) dissolution profiles of (**A**) Lasix, (**B**) generic furosemide, (**C**) pure drug, and (**D**) lyophilized formula, fitted using the Korsmeyer–Peppas model.*

ity, with the lyophilized product showing the greatest deviation.

DISCUSSION

The present study evaluated the impact of lyophilization on the solubility and dissolution performance of furosemide, a BCS class IV drug characterized by poor aqueous solubility and limited intestinal permeability. The findings demonstrated that lyophilization significantly improved both the solubility and dissolution rate of furosemide when compared to the pure drug, the reference product (Lasix), and a marketed generic formulation.

The marked increase in solubility observed for the lyophilized formulation may be attributed to several physicochemical modifications introduced by lyophilization, including increased porosity, reduced crystallinity, enhanced wettability, and improved particle dispersion. Comparable results have been reported in prior investigations, indicating that freeze-drying markedly enhances the solubility of weakly water-soluble pharmaceuticals (*19–21*).

The rapid release of the lyophilized formulation can be attributed to its highly porous matrix, increased surface area, reduced particle aggregation, and possible partial amorphization of the drug substance. These factors facilitate improved water penetration and accelerated drug dissolution (*22*, *23*).

The superiority of the Korsmeyer–Peppas model was confirmed as the best fit model for describing the release profiles. These findings are consistent with previous reports indicating that lyophilized systems favor diffusion-based release due to their porous structure (*24*).

Despite its superior dissolution performance, the lyophilized formulation exhibited an f_1 value of 162.23 when compared to Lasix, exceeding the FDA's similarity threshold ($f_1 \leq 15$). This confirms a substantial dissimilarity between the release profiles of the lyophilized product and the reference formulation. Therefore, although lyophilization markedly improves solubility and dissolution, it does not guarantee pharmaceutical equivalence without further in vivo bioequivalence assessments. Only the generic formulation demonstrated acceptable similarity to Lasix (f_1 = 8.45), as expected for an approved interchangeable product.

A key strength of this study is the successful application of lyophilization to substantially enhance the dissolution rate of furosemide, providing a promising strategy for improving oral delivery of BCS class IV drugs. Unlike most previous studies that relied primarily on solid dispersions or cyclodextrin complexes, this work demonstrates a process-driven enhancement approach. The comprehensive comparative analysis with both the reference (Lasix) and a marketed generic product allowed for a robust and clinically relevant evaluation of the formulation's performance. Collectively, these findings underscore the novelty of applying lyophilization as a formulation strategy for furosemide and highlight its potential significance as a platform technology for improving the biopharmaceutical properties of other poorly soluble drugs.

Despite these improvements, the lyophilization process yielded a powder that was stored in type I glass vials, serving as a proof-of-concept rather than a finished dosage form. The lyophilized product remained visually stable during short-term storage under desiccated conditions, showing no evidence of collapse, shrinkage, or discoloration. In contrast, Lasix and the generic tablets were commercially packaged with established stability data. Thus, accelerated and long-term stability studies are required to comprehensively evaluate the stability of the lyophilized formulation. Moreover, the study is limited by its exclusive reliance on in vitro data. Further in vivo pharmacokinetic and pharmacodynamic studies are necessary to assess the clinical relevance and ensure the biopharmaceutical safety and efficacy of the lyophilized formulation.

CONCLUSION

In this study, lyophilization proved to be an effective strategy to enhance the solubility and dissolution rate of furosemide, a poorly water-soluble BCS class IV drug. The lyophilized formulation demonstrated significantly faster drug release compared to both the pure drug and commercially available products, and the release profiles for the lyophilized product and the reference formulation lacked similarity.

DISCLOSURES

The authors received no financial support for this work and have no conflicting interests.

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Bibliometric Study of Trends in Chemometrics Applied to Drug Dissolution Testing

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ABSTRACT

This bibliometric study explores the multifaceted domain of the dissolution of solid oral pharmaceutical forms, focusing on key aspects such as dissolution testing, dissolution profiling and modeling, and comparative dissolution tests for therapeutic equivalence over the past 40 years (1982–2025). The pharmaceutical quality system hinges on controlling the product and process elements. Dissolution tests are critical for bioperformance and therapeutic equivalence, necessitating mastery of this domain and the influencing factors. Traditionally, these procedures rely on liquid chromatography and UV-visible spectroscopy, which are often cumbersome and generate significant waste. However, innovative techniques such as artificial intelligence, machine learning, and chemometrics are gaining prominence, especially in research laboratories and institutions involved in pharmaceutical development. Pharmacopoeias contain general chapters on chemometrics and associated guidelines, including those from the Official Medicines Control Laboratories (OMCL) network, which develops chemometric tools for quality control, even for counterfeit products. Regulatory bodies like the ICH and authorities in developed countries encourage the pharmaceutical industry to adopt next-generation practices, including quality by design (QBD), process analytical technology (PAT), and continuous manufacturing. The development of increasingly complex drugs drives the adoption of new tools to address performance, structural complexity, excipient effects, and multicomponent formulations. These innovations aim to enhance the precision and efficiency of dissolution methods while reducing environmental impact and associated costs. Integrating advanced tools like chemometrics allows researchers to obtain more reliable results and optimize drug development processes. The future of the pharmaceutical industry relies on adopting these cutting-edge technologies to ensure superior product quality and meet growing regulatory demands.

KEYWORDS: chemometrics, dissolution testing, bibliometric analysis, pharmaceutical quality control

INTRODUCTION

The field of dissolution of solid oral dosage forms encompasses several key aspects essential to ensuring drug quality and efficacy. These aspects include dissolution testing, dissolution profile modeling, and comparative dissolution testing in the context of therapeutic equivalence (*1*, *2*).

Traditionally, dissolution testing has relied primarily on liquid chromatography and UV-visible spectroscopy. These methods, while robust and widely used, can be procedurally intensive and generate significant amounts of waste. This poses environmental and logistical challenges for laboratories (*3*).

However, innovative techniques such as artificial intelligence (AI), machine learning, and chemometrics have started gaining importance. These technologies offer new opportunities to improve the efficiency of dissolution testing, reduce waste, and optimize

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processes. Chemometrics is the science of extracting relevant information from chemical systems by using data-driven mathematical and statistical methods. AI and machine learning can analyze large datasets to identify trends and predict drug behavior, improving the accuracy and efficiency of dissolution methods (*4–8*).

The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) and authorities in developed countries are encouraging manufacturers to adopt the next generation of pharmaceutical manufacturing. This includes concepts such as quality by design (QBD), process analytical technology (PAT), and continuous manufacturing. Dissolution testing is a key element of bioperformance and therapeutic equivalence, making mastery of this area and the factors that influence it crucial (*9–13*).

It is important to note that pharmacopoeias contain general chapters on chemometrics and associated guidelines. In particular, the Official Medicines Control Laboratories (OMCL), which is a network of control laboratories, is developing the application of chemometrics tools for quality control, including for counterfeit products. These guidelines provide frameworks for the rigorous and systematic application of these innovative methods (*14*).

The development of increasingly complex drugs is driving the adoption of new tools to address issues of performance, structural complexity, the effect of excipients, and management of multicomponent formulations. These innovations aim to improve the precision and efficiency of dissolution methods. Advanced techniques such as Raman spectroscopy and artificial neural networks offer more sophisticated and precise means of analysis. These tools allow researchers to obtain more reliable results and better understand the interactions between the different components of formulations (*4*, *15–18*). By integrating advanced tools such as chemometrics, researchers can reduce the environmental impact of dissolution testing by minimizing the waste generated. Additionally, these technologies can help reduce testing costs by automating and optimizing processes (*19*).

The future of the pharmaceutical industry depends on the adoption of these cutting-edge technologies to ensure superior product quality and meet increasing regulatory requirements. Integrating AI, machine learning, and chemometrics into dissolution testing not only improves the accuracy and efficiency of existing methods but also creates new opportunities for innovation and the development of more complex and personalized drugs. This evolution is essential to meet the ever-growing needs of both patients and the pharmaceutical industry (*20*, *21*).

This bibliometric study aims to analyze and map the scientific literature to identify and visualize evolving trends, key research areas, and the collaborative landscape in the application of chemometrics to drug dissolution testing.

METHODS

To achieve our research objective, we developed our keyword search to comprehensively cover the topic. The search key consists of three main components:

1. **Chemometrics Component**: ("Chemometric" OR "Chemometrics" OR "Multivariate" OR "Least Squares" OR "Partial least squares discriminant analysis" OR "Inverse Least Squares" OR "Principal Components Regression" OR "Partial Least Squares Regression" OR "Artificial Neural Networks" OR "Locally Weighted Regression" OR "Principal component analysis" OR "cluster analysis" OR "k-Nearest neighbors" OR "Multivariate curve resolution" OR "Soft independent modeling of class analogy" OR "Multiple linear regression" OR "Multiplicative scatter correction")

2. **Dissolution Component:** ("Drug release" OR "Dissolution" OR "Dissolution test" OR "Dissolution testing" OR "Dissolution profile")

3. **Analytical Methods Component:** ("Spectrophotometry" OR "spectroscopy" OR "Spectrometry" OR "Infrared" OR "Near infrared" OR "Raman" OR "fluorescence" OR "Nuclear magnetic resonance" OR "Fiber optic" OR "chromatography" OR "Electrochemical" OR "Voltammetry" OR "Electroanalytical")

This approach covers a wide range of relevant topics, including chemometric techniques, dissolution tests, and the various analytical methods used in this field. By including these three components, the search captured the most relevant studies (*22*).

The PRISMA flow diagram (Fig. 1) outlines the study selection process for the bibliometric review, beginning with 1449 articles identified through the Scopus database. Initial screening applied the following inclusion criteria: subject area = pharmacology, toxicology, and pharmaceutics; document type = article; publication date between Feb 5, 1982 and Feb 22, 2025; and language = English. After excluding articles that did not meet these

criteria (966 articles), 483 articles underwent eligibility assessment, and 170 full-text articles were excluded due to insufficient information or irrelevance to the study focus. A total of 313 full-text articles were included in the final review.

The analysis was organized using the following structure: intellectual (publications, authors, and citations), social (institutions and countries), and conceptual (keywords).

RESULTS AND DISCUSSION

Figure 2 illustrates the annual production of scientific articles over the 40-year period from 1982–2025, with a variation ranging from 0 to 25 articles per year. Over time, an increase in the number of published articles can be seen, with a growing interest in the field of dissolution and chemometrics since 2020. This upward trend reaches a notable peak around 2020, when the number of published articles peaks. After 2020, the annual production of articles stabilized at around 20 articles per year. This stabilization can be interpreted as a sign of maturation of the field. Indeed, with the majority of basic concepts having been extensively explored, research is now focusing on more specific aspects or innovative applications of dissolution and chemometrics.

Intellectual Structure

The analysis of the intellectual structure of the field of dissolution and chemometrics revealed a rich interconnectedness of contributions from influential

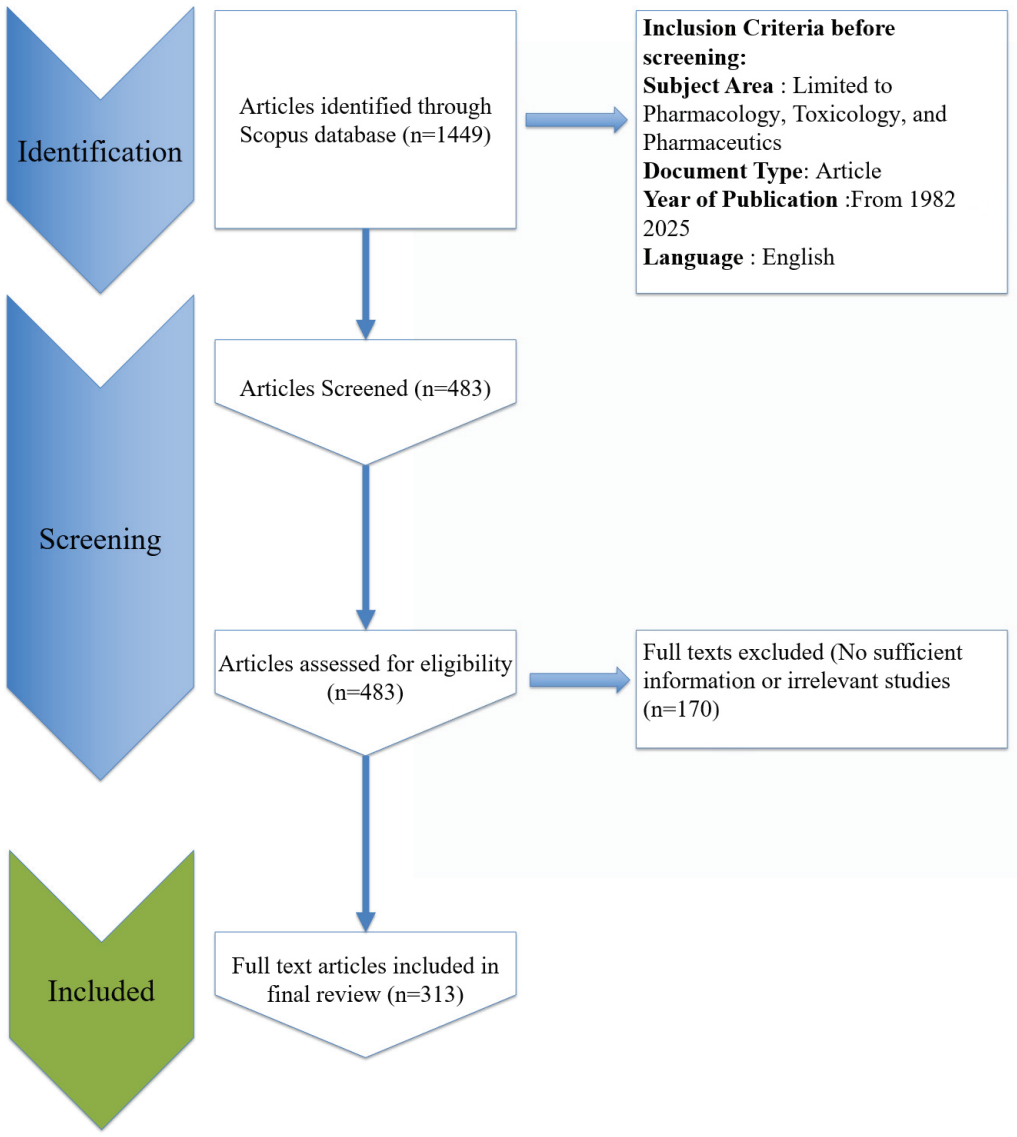

Figure 1. PRISMA Flow Diagram of Literature Search and Selection Process for Studies on Dissolution Testing of Solid Oral Pharmaceuticals (1982–2025).

authors, leading journals, and landmark articles. This sheds light on how knowledge has been developed and disseminated, and the findings identify the authors and journals that play a central role in advancing research.

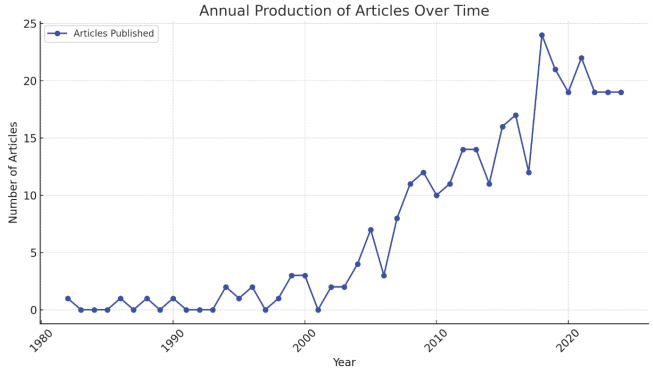

Figure 2. Number of relevant publications per year from Feb 1982–Feb 2025.

Authors and Their Influence

The analysis of intellectual structure begins with the identification of influential authors. Analyzing their collaborations can also reveal important research networks and co-authorship dynamics. In this field, Zsombor Kristóf Nagy, Attila Farkas, and Mansoor A. Khan stand out, with a total of 14, 12, and 12 publications, respectively (Fig. 3). Their contributions reflect not only their influence but also their ability to mobilize and guide research in dissolution testing and chemometrics. Their work is frequently cited and forms a reference base for other researchers.

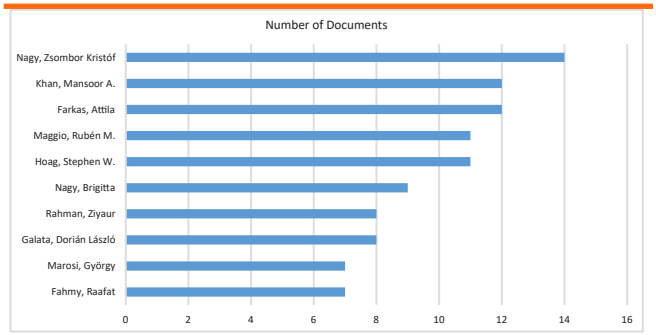

Figure 3. Most relevant authors based on cumulative number of publications in the field from Feb 1982–Feb 2025.

Dominant Sources and Journals

Scientific journals play a crucial role as platforms for knowledge dissemination. Among the most influential sources in this field, the *International Journal of Pharmaceutics* stands out with a total of 55 published articles (Fig. 4). This journal is a key source for researchers, providing cutting-edge research and critical reviews that shape the understanding and practical applications of dissolution and chemometrics.

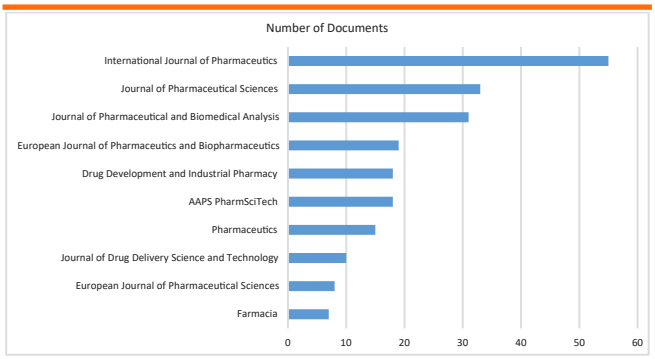

Figure 4. Most relevant journals based on cumulative number of publications in the field from Feb 1982–Feb 2025.

The *Journal of Pharmaceutical Sciences*, with 33 articles, and the *Journal of Pharmaceutical and Biomedical Analysis*, with 31 articles, are also leading journals (Fig. 4). Their significant contribution demonstrates their central role in disseminating knowledge and innovations in this field.

Key Articles and Their Impact

Some publications have a particularly strong impact and mark significant advances in the field. For example, the article by Goyanes A, published in 2015 in the journal *Molecular Pharmaceutics*, has been cited 440 times (Fig. 5a), demonstrating its influence and importance in subsequent research (*23*). This article appears to have introduced innovative concepts or crucial methodologies that have been widely adopted and cited by other researchers. Similarly, Kirsch JD's 1995 article in the *Journal of Pharmaceutical and Biomedical Analysis*, with 134 citations (Fig. 5a), is another pillar of the field (*24*). These key articles demonstrate how certain research projects can define paradigms and influence generations of scientific work.

Figure 5b provides a comprehensive overview of the cumulative number of publications in the field for the top five pharmaceutical journals from 1982–2025. Over the years, there has been a noticeable increase in publications, particularly after 2000. The *International Journal of Pharmaceutics* has the most publications, followed by the *Journal of Pharmaceutical and Biomedical Analysis*. The other journals—*AAPS PharmSciTech*, *European Journal of Pharmaceutics and Biopharmaceutics*, and *Journal of Pharmaceutical Sciences*—also show an upward trend, but with fewer publications than the top two journals. These data highlights the growing productivity and publication trends in pharmaceutical research over the past 20 years.

Social Structure

The social structure in the field of dissolution and chemometrics focuses on examining the relationships and

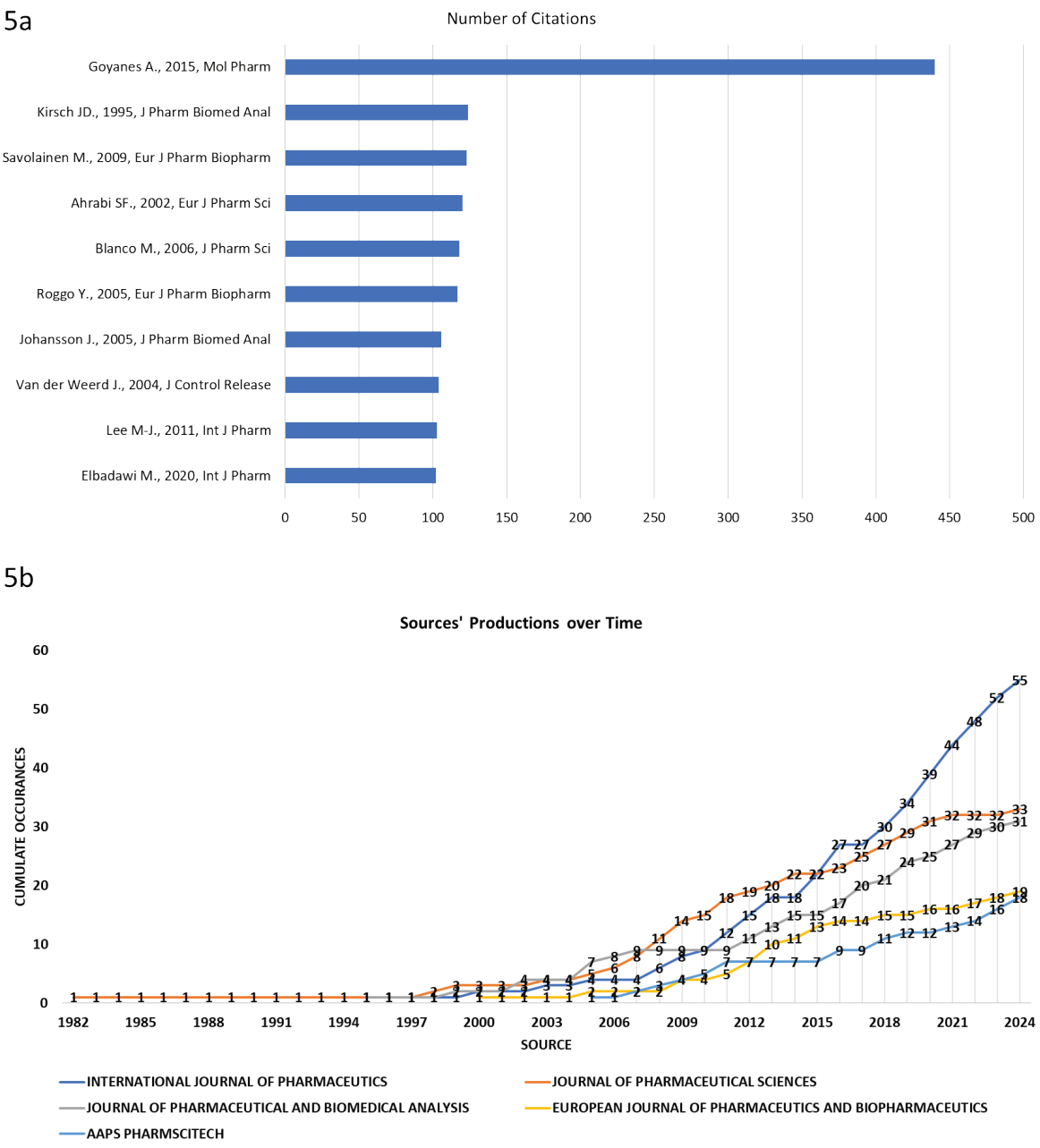

*Figure 5. Most relevant publications and journals based on cumulative number of citations (**a**) and publications (**b**) in the field from Feb 1982–Feb 2025.*

levels of scientific collaboration between institutions and countries. This analysis sheds light on how collaborative networks influence the production and dissemination of knowledge.

Collaborations Between Authors

Nagy, Zsombor Kristóf, and Farkas, Attila are prominent examples of authors with extensive collaborations, with 14 and 12 co-authored papers (Fig. 3), respectively. These collaborations reflect well-established networks, where authors share their expertise and work together to advance the field. Such networks are essential for stimulating innovation and facilitating the resolution of complex problems through a synergy of ideas and skills.

Institutional Networks

In terms of institutional networks, collaborations between various research institutions reveal the most influential centers in the field. These interinstitutional collaborations are often the result of strategic partnerships aimed at combining resources and expertise for ambitious research projects. Leading institutions serve as hubs of innovation and training, attracting researchers from diverse backgrounds and strengthening their global influence.

Collaborations Between Countries

At the country level, some nations stand out for their international collaborations. The United States, for example, demonstrates close collaborations with the United Kingdom, Canada, and Australia. These partnerships reflect cultural and linguistic affinities, as well as shared scientific interests. In Europe, countries such as Germany, France, Italy, and Spain also demonstrate strong regional collaborations, often supported by European funding programs.

In Asia, countries such as China, Japan, South Korea, and India demonstrate growing collaborations both regionally and internationally. These collaborations demonstrate the growing importance of scientific research in Asia and the integration of these countries into the global network of dissolution and chemometrics research.

Overall, the analysis of the social structure in the field of dissolution and chemometrics highlights the importance of collaborative networks at different levels. Relationships between authors, institutions, and countries play a crucial role in the production and dissemination of knowledge, and these collaborations are essential for the continued advancement of the field.

Conceptual Structure and Gaps

The conceptual framework aims to map the landscape of dominant concepts, theories, and paradigms in the field of dissolution and chemometrics. It examines the relationships between different keywords that appear in the literature to structure knowledge and identify potential gaps.

Several concept clusters were identified (Fig. 6). These include pharmaceutical technology and process control, advanced methods to improve drug solubility, physiochemical properties of drugs, and emerging technologies such as 3D printing.

Analysis of the conceptual structure (Fig. 6) also helps identify gaps in current research. For example, there is a need for additional research on the application of artificial intelligence (AI) in pharmaceutical processes. Furthermore, excipient variability is another area requiring in-depth study to better understand and control their impact on drug quality and efficacy.

Future Directions

The future of the field of dissolution and chemometrics relies on the integration of new technologies and innovative approaches. These advances promise not only to optimize manufacturing processes but also to revolutionize the personalization and efficiency of pharmaceutical treatments.

Artificial Intelligence and Machine Learning

The use of AI and machine learning is a promising avenue for optimizing pharmaceutical manufacturing processes. AI can analyze large data sets to identify trends and anomalies, enabling better quality management and reduced production costs. Machine learning algorithms can also predict the behavior of drugs and excipients, facilitating the development of more effective and safer formulations (*25–30*).

Personalization and 3D Printing of Drugs

Innovation in drug personalization, particularly through 3D printing, offers tailor-made solutions to meet individual patient needs. 3D printing makes it possible to manufacture drugs with specific dosages, shapes, and controlled releases, tailored to each patient. This technology could transform the way treatments are prescribed and administered, offering unparalleled precision and personalization (*31–35*).

Development of New Excipients

The development of new excipients is essential to improve the stability and bioavailability of drugs. Excipients play a crucial role in drug formulation, influencing their dissolution, absorption, and efficacy. Innovation in this area can lead to more stable formulations with improved release of active ingredients, and to more effective and safer drugs (*36*).

Advanced Techniques

The adoption of advanced techniques, such as Raman spectroscopy and artificial neural networks, is also a promising direction for the future of this field. Raman spectroscopy can provide detailed information on chemical composition and molecular interactions, and artificial neural networks can model complex systems and predict formulation outcomes. These advanced technologies offer new perspectives for pharmaceutical research and development (*4, 7, 14–16*).

By integrating these new technologies and approaches, the field of dissolution and chemometrics is poised to enter a new era of innovation and efficiency. The future promises personalized solutions, optimized processes, and safer and more effective drugs, meeting the ever-growing needs of patients and the pharmaceutical industry.

Research Limitations

This study has limitations. First, although the Scopus

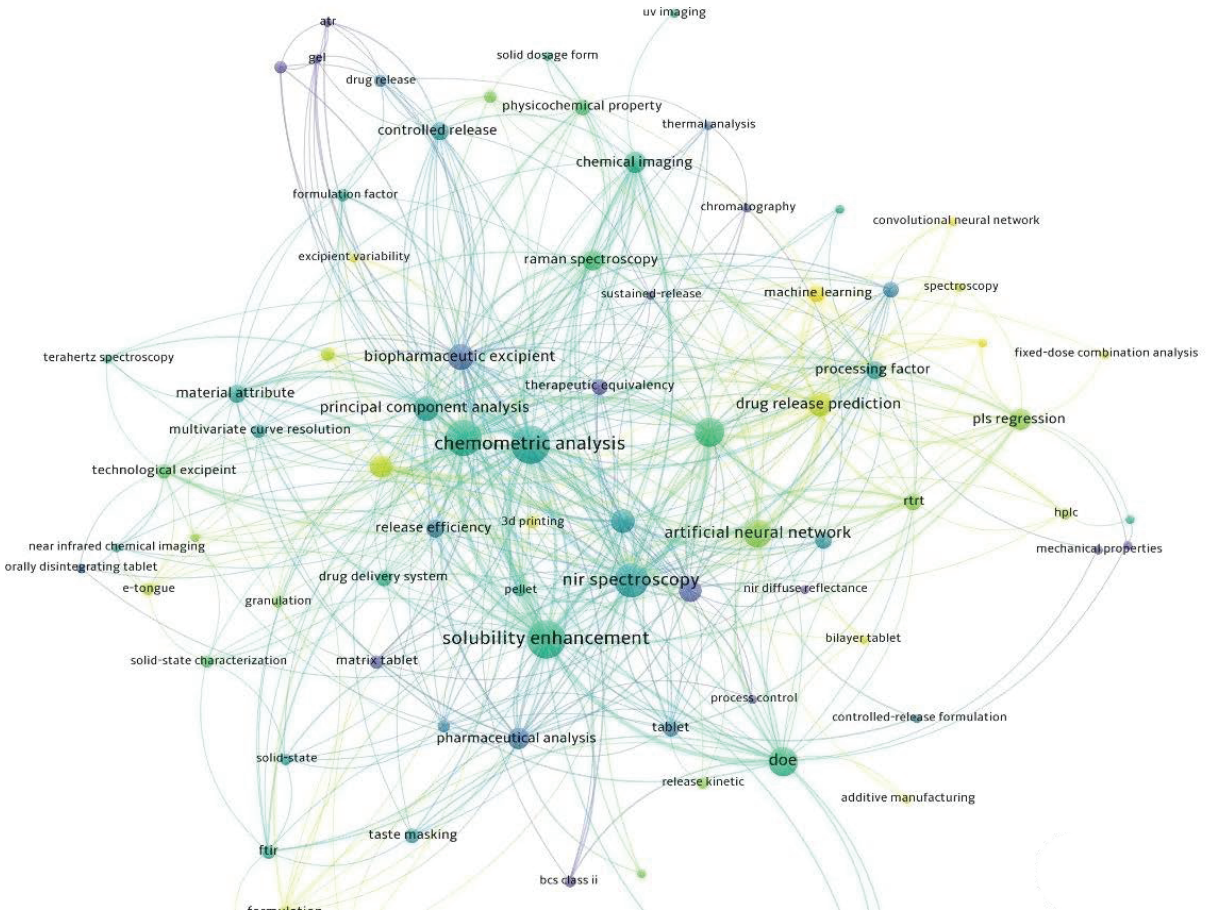

Figure 6. Network diagram of authors' co-occurring keywords in dissolution testing over time based on literature analysis (1982–2025).

- ***Blue**: The blue cluster includes terms such as "release testing" and "tablet" and focuses primarily on pharmaceutical technology and process control. This cluster explores the methods and practices used to test drug release and ensure the quality of pharmaceutical products.*
- ***Green**: The green cluster is characterized by keywords such as "solubility enhancement" and "chemometric analysis." It highlights pharmaceutical analysis and the use of advanced methods to improve drug solubility. This cluster underlines the importance of chemometric analysis in understanding and optimizing the pharmaceutical properties of compounds.*
- ***Yellow**: The yellow cluster focuses on the physicochemical properties of drugs and emerging technologies, such as 3D printing. This cluster explores new technologies and methods for manufacturing drugs with specific properties, as well as the challenges associated with these innovations.*

database covers the majority of studies concerning our topic, other databases such as Medline (PubMed) and Web of Science may contain additional publications. Therefore, although this study represents a robust and significant image of the literature on the topic, it may not represent entirety the research in the field of chemometrics applied to dissolution testing.

CONCLUSION

The study highlights the evolution and future directions in the field of dissolution and chemometrics. Traditional methods, though effective, present environmental and logistical challenges. The introduction of AI, machine learning, and chemometrics provides new opportunities to improve efficiency, precision, and sustainability in dissolution testing. Regulatory encouragement for practices such as QbD, PAT, and continuous manufacturing underscores the need for a robust pharmaceutical quality system. Mastery of dissolution testing remains crucial for ensuring bioperformance and therapeutic equivalence. The role of pharmacopoeias and guidelines in standardizing these advanced techniques cannot be overstated. The development of complex drugs requires innovative approaches to address various challenges, from performance to structural complexity and excipient variability. By integrating advanced tools, researchers can achieve more reliable outcomes, optimize drug development processes, and reduce environmental impact. The future of pharmaceutical research and manufacturing will undoubtedly be shaped by the adoption of these technologies, ensuring superior quality products and compliance with stringent regulatory

requirements. This study underscores the importance of continuous innovation and adaptation to meet the evolving needs of the industry and patients alike.

DISCLOSURES

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2025 AAPS 360 Annual Meeting: Highlights in In Vitro Release and Dissolution Testing and Oral Biopharmaceutics Modeling

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ABSTRACT

This manuscript highlights key sessions from the In Vitro Release and Dissolution Testing (IVRDT) and Oral Biopharmaceutics and Absorption Modeling (OBAM) communities at the 2025 AAPS PharmSci 360 Annual Meeting (November 9–12, San Antonio, TX). Presentations emphasized a shift toward mechanistic and predictive in vitro and in silico tools, including enzymatic dissolution media, physics-based particle dissolution modeling, physiologically based biopharmaceutics modeling (PBBM) applications for food-effect assessment and specification setting, advanced gastrointestinal simulation platforms, AI-driven formulation optimization, and the complementary role of preclinical animal studies. Collectively, these sessions underscored the value of integrating biorelevant experimentation with computational modeling to streamline and de-risk oral drug development.

KEYWORDS: In vitro release and dissolution testing (IVRDT), oral biopharmaceutics and absorption modeling (OBAM), biorelevant dissolution, biopredictive, physiologically based biopharmaceutics modeling (PBBM), dissolution modeling

INTRODUCTION

The American Association of Pharmaceutical Scientists (AAPS) successfully hosted its PharmSci 360 Annual Meeting and Exposition from November 9–12, 2025, at the San Antonio Convention Center in San Antonio, TX. As one of the premier global gatherings for pharmaceutical scientists, this event fosters collaboration among experts from academia and industry (Fig. 1).

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#Tahseen Mirza did not attend the AAPS 360 meeting but contributed as the Chairman of the IVRDT Community in organizing, topics selection, and in manuscript review.

This year, the In Vitro Release and Dissolution Testing (IVRDT) and Oral Biopharmaceutics and Absorption Modeling (OBAM) communities played an especially meaningful role by recommending a curated selection of scientific sessions, emerging hot topics, and keynote speakers. These recommendations were thoughtfully developed in direct response to the needs and priorities expressed by their community members, ensuring that the programming addressed the most current, relevant, and pressing scientific challenges. The resulting sessions not only highlighted cutting edge advancements but also reflected the collective interests and values of these vibrant scientific communities. In this highlight manuscript, we provide a concise summary of the presentations, discussions, and scientific advancements featured in these community driven sessions. Our goal is to capture and disseminate the key insights shared by the speakers, with a particular focus on the topics most relevant to the IVRDT and OBAM communities. By doing so, we aim to amplify the knowledge exchanged at PharmSci 360 and support continued learning across our scientific networks.

Industrial and academic presenters discussed topics related to advancing biorelevant dissolution and absorption prediction by integrating in vitro, in silico and mechanistic modeling approaches with preclinical and clinical studies. Speakers highlighted how enzymatic effects, formulation design, and dosage-form–specific behavior (e.g., amorphous solid dispersions and orodispersible tablets) influence dissolution and downstream exposure. A strong theme was the expanding role of PBPK/PBBM to link dissolution to systemic and local gastrointestinal (GI) drug performance, including case studies on food effects, specification setting, and locally acting drugs like mesalamine. Several presentations examined current

Figure 1. Photo captured at the IVRDT dinner during PharmSci 360 (November 2025) along the San Antonio Riverwalk. Left side: Niloufar Salehi, Vivian Gray, Aleksander Mendyk, Ishai Nir, and Sanjaykumar Patel. Right side: Andre Herman, Nikoletta Fotaki, Mark Liddell, Jie Shen, Pradnya Bapat, Alger Salt, and Zhao Liu.
IVRDT: In Vitro Release and Dissolution Testing.

gaps, advances, and future opportunities in mechanistic dissolution modeling and computational analysis. Overall, the talks emphasized a shift toward predictive, mechanistic in vitro and in silico tools to de-risk oral drug development.

This report highlights some of the main hot topics, symposiums, and keynote presentations, including the following:

Rapid Fire Sessions:

- Enhancing biorelevance: unveiling enzymatic impact on simulated GI dissolution
    - *Catarina I. D. Chendo, MS, Hovione*
- In vitro + in silico: advanced tools for absorption prediction
    - *Balint Sinko, PhD, Pion Inc*

Hot Topic Session:

- Identifying gaps and pushing boundaries in mechanistic dissolution modeling
    - *Deanna M. Mudie, PhD, Simulations Plus, Inc*
    - *Yanxing Wang, PhD, New Mexico State University*
    - *Jozef Al-Gousous, PhD, Johannes Gutenberg University Mainz and University of Michigan*

Symposium Sessions:

- Advanced in vitro GI simulation and physiologically-based biopharmaceutics modeling (PBBM) to support oral drug development
    - *Connor O'Farrell, PhD, InnoGI Technologies*
- Advances in computational analysis of dissolution (ASD)
    - *Rob Tzuchi Ju, PhD, Abbvie Inc.*
- Advances in computational analysis of dissolution: orodispersible tablets
    - *Aleksander Mendyk, MSC, PhD, DSC, Jagiellonian University Medical College*
- De-risking formulation strategies using PBBM: mechanistic case studies on evaluating food effects and guiding dissolution specifications
    - *Deanna M. Mudie, PhD, Simulations Plus, Inc.*
- Mechanistic PBPK modelling for the locally acting git drug: mesalamine
    - *David B. Turner, PhD, Certara Predictive Technologies, Certara UK Limited*

Keynote Session:

- Current status and future perspective of pre-clinical in vivo studies vs in vitro/in silico predictive biopharmaceutics tools
    - *David C. Sperry, PhD, Eli Lilly and Company*

RAPID FIRE SESSIONS

Catarina Chendo addressed limitations of conventional biorelevant dissolution methods that excluded digestion by developing an improved simulated GI dissolution approach that integrates enzymatic digestion and food effects to better reflect human physiology. Pepsin and pancreatin were incorporated into fasted and fed simulated gastric and intestinal fluids, and enzymatic activity was confirmed using protein substrates that showed rapid digestion under fasted conditions and slower, pH dependent digestion in fed media. Two case studies with USP apparatus 2 demonstrated the impact on dissolution: a spray dried lysozyme formulation showed rapid release in enzyme free fasted media but substantial loss in enzyme containing media due to proteolysis, highlighting limitations of enzyme free methods for protein based drugs, whereas an itraconazole amorphous solid dispersion with a protein excipient exhibited enhanced intestinal dissolution in the presence of enzymes due to matrix cleavage. Overall, the enzyme integrated method captured both enzymatic degradation and food effects, improving the physiological relevance and translational value of in vitro dissolution data for formulation design and early development decisions.

Dr. Balint Sinko focused on key learnings from the development and evaluation of advanced formulation strategies for poorly soluble BCS Class II and IV compounds, highlighting how dissolution permeation (flux) assays combined with physiologically relevant mechanistic modelling improved understanding of oral absorption. While advanced approaches such as amorphous solid dispersions and nanonization enhanced apparent solubility, the case studies showed that flux data alone were insufficient to predict in vivo performance due to factors such as limited membrane geometry and particle drifting. Integrating modelling with in vitro data enabled identification of rate limiting absorption

steps, clarification of dose dependent shifts between dissolution-limited, permeability-limited, and solubility limited absorption, and reconciliation of apparent in vitro differences with observed in vivo bioequivalence. Overall, the presentation demonstrated that coupling flux assays with mechanistic modelling strengthened in vitro–in vivo translation, reduced formulation selection risk, and supported more confident progression toward clinical evaluation.

HOT TOPIC SESSION

The hot topic moderated by Dr. Deanna Mudie and panelists addressed the gap between empirical dissolution approaches and the need for mechanistic understanding when dissolution interacts with complex physiological processes. Dissolution was shown to be a critical determinant of oral bioavailability for poorly soluble drug products, and although in vitro–in vivo correlation methods linked dissolution to systemic exposure, they often lacked explanatory power. Mechanistic dissolution modeling was highlighted as a way to describe the underlying physical and chemical processes using measurable drug, formulation, and GI properties, enabling identification of key performance attributes, optimization of release profiles, linkage of in vitro and in vivo dissolution, and support for setting dissolution specifications (*1*, *2*). When integrated within physiologically based biopharmaceutic modeling (PBBM) frameworks that capture GI transit, permeation, distribution, metabolism, and excretion, mechanistic dissolution models can support prediction of pharmacokinetics across populations (*3*). Many existing mechanistic and semi-mechanistic models have shown utility in predicting in vitro and in vivo dissolution (*4*, *5*). However, improvements can be made to increase applicability since many are specific to particular in vitro setups and/or conflate multiple effects, such as shear and convection, limiting generalizability. Such approaches can cause difficulties in translating between in vitro and in vivo conditions, particularly for particles larger than 20 µm in radius, and/or large aspect ratios dissolving in nonquiescent environments (*5*, *6*). Furthermore, increased understanding of convection-enhanced diffusion and electrochemical gradients is needed to improve prediction accuracy of weakly basic drug dissolution in unbuffered media representative of the fasted stomach. This hot topic session highlighted recent advances aimed at overcoming these challenges, including improved prediction of ionizable drug dissolution in unbuffered media and physics-based approaches that explicitly account for particle shape, polydispersity, and fluid hydrodynamics in both in vitro and in vivo contexts.

Dr. Yanxing Wang presented a physics-based framework that advances mechanistic dissolution modeling by moving beyond the oversimplified assumption of spherical drug particles in idealized flows. The work demonstrates that non-spherical particle geometry alone even under inertia-free creeping-flow conditions generates complex, quasi-periodic, and chaotic rotational dynamics in triaxial ellipsoidal particles, directly impacting surface renewal and local mass transfer. When weak inertia is introduced, the transient evolution toward stable rotational states produces structured, time-dependent flow fields that significantly alter convective transport near the particle surface. For sharp-edged cuboidal particles, which better represent real pharmaceutical solids, edges and corners act as micro-stirrers inducing localized vortices and flow separation that create enhanced and distinct mass transfer pathways. At the intestinal scale, peristaltic wave models revealed that cooperative interaction between two waves can drive chaotic mixing even at very low Reynolds numbers, with tunable wave parameters controlling the location and intensity of mixing suggesting the body may actively regulate dissolution and absorption through coordinated muscular contractions. Together, this work links particle geometry, weak inertia, and intestinal hydrodynamics into a unified mechanistic framework for more physiologically relevant dissolution prediction. The authors gratefully acknowledge Dr. Niloufar Salehi and Dr. Youlin Liu of Eli Lilly and Company for their valuable insights and constructive discussions. This work was supported by the National Science Foundation ERI Program (award no. 2138740) and CAREER Program (award no. 2443848).

Dr. Jozef Al-Gousous challenged the long-standing stagnant film dissolution models by demonstrating that both the thermodynamic approach and the Mooney et al. model produce large systematic errors in unbuffered reactive media, with three- to four-fold underestimation and two- to three-fold overestimation of experimental fluxes, respectively, for weakly basic drugs (*7*). These errors stem from the fundamental difference between convective diffusion and stagnant film diffusion in their sensitivity to diffusivity discrepancies among reacting species. Numerically solving the comprehensive convection-diffusion-reaction (CDR) equation reduced prediction errors to under 20%, and analytical solutions were further derived for two physiologically relevant limiting cases: high background electrolyte (in vivo gastric) and zero background electrolyte (in vitro regulatory media), offering computational simplicity

without sacrificing accuracy. Key findings revealed that proton diffusion from bulk to interface, not drug diffusion away from it, is the rate-limiting step in weak base gastric dissolution, and that convection actively influences surface pH, contradicting conventional assumptions. For suspended particles, surface pH was shown to depend on both particle size and agitation rate, underscoring the need for accurate fluid dynamic models to predict dissolution of real pharmaceutical particles with complex geometries.

SYMPOSIUM SESSIONS

Dr. Connor O'Farrell demonstrated the integration of the TIM platform of advanced in vitro GI models with PBBM to support oral drug development (*8*). While compendial USP apparatus remain appropriate for quality control, the tiny-TIM and TIM-1 models of the upper GI tract provide greater biopredictive capability for compounds whose solubility is sensitive to dynamic luminal conditions such as pH fluctuations, bile micelle formation and concentration, and the generation of digestion products during GI transit. Three complementary integration strategies were outlined: biopredictive dissolution input, mechanistic model parameterization, and evidence-based biopharmaceutics risk assessment. Firstly, a biopredictive dissolution case study combining TIM-1, TIM-2, and GastroPlus for a modified-release formulation of a BCS II compound showed how intrinsic dissolution variability under the fixed physiological conditions of TIM could support interpretation of clinical pharmacokinetic (PK) variability. Secondly, a case study demonstrated that while tiny-TIM correctly predicted food effects for 20/22 compounds across all BCS classes, the two incorrect predictions for atenolol and metformin were resolved by combining TIM data with GastroPlus to mechanistically model membrane transporters and permeability (*9*). Finally, when applied as a novel biopharmaceutics bridging risk assessment (BBRA) tool, a combined TIM-PBBM approach has been projected to reduce in vivo bridging studies by 70% (*10*). This highlights the potential power of integrating advanced in vitro and in silico tools as a comprehensive biopharmaceutics toolbox.

Dr. Rob Tzuchi discussed an internally developed biopredictive two-stage dissolution methodology for evaluating amorphous solid dispersion (ASD) performance without surfactants, where amorphous solubility and formulation robustness govern in vitro release. High rotational speeds (125 rpm) and mechanical shear via fluted disks were critical for success, particularly for erosion-based formulations, while an optimal filter size of 70 µm yielded the strongest in vitro–in vivo correlation, challenging the liquid-liquid phase separation (LLPS) nanoparticle assumption. The method demonstrated robust correlation with in vivo performance across multiple ASD platforms and conventional crystalline formulations, with sensitivity to batch-to-batch and supplier variability. Concurrent release of drug and functional excipients emerged as a potential surrogate marker for favorable bioavailability, while micro-CT imaging during dissolution provided complementary mechanistic insights into gel layer formation. Together, these analytical approaches were operationalized into a risk assessment matrix assigning risk levels to critical material attributes (CMAs), formulation variables (CFVs), and process parameters (CPPs) to guide method development and formulation design at AbbVie.

Prof. Aleksander Mendyk presented the application of artificial intelligence to optimize the development of orodispersible tablets (ODTs), which are valued for their near-instantaneous oral disintegration. He highlighted AI's unique capability to integrate multidimensional knowledge sources while remaining accessible through high-availability AutoML tools that no longer require specialized modeling expertise, a critical advantage given the vast landscape of excipients, manufacturing technologies, and equipment involved in ODT development. A case study demonstrated the use of automated machine learning (AutoML) to build predictive models for ODT disintegration time, emphasizing data quality as a prerequisite for model success. SHAP analysis of the best-performing model enabled meaningful knowledge extraction, providing qualitative validation aligned with domain expert understanding and demonstrating AI's potential to generalize knowledge and serve as a development guide. Prof. Mendyk concluded by integrating the ODT disintegration model into a larger modeling framework aimed at predicting drug release from modified-release ODTs, underscoring the broader impact of AI-driven decision support systems in streamlining formulation development and process optimization. Prof. Mendyk acknowledged his co-workers and both IVRDT and OBAM communities for the smooth and fruitful collaboration.

Dr. Mudie discussed two mechanistic case studies demonstrating how PBBM can elucidate food effects and guide dissolution specifications, reducing reliance on clinical studies. In the first case study, PBBM was applied to selumetinib, a weakly basic salt formulated as an immediate-release capsule and enteric-coated granules, revealing that the capsule's negative food effect stemmed from reduced dissolution and increased precipitation

in the higher-pH fed stomach, while enteric-coated granules were protected by delayed release after gastric emptying (*11*). Critically, the validated model defined a dissolution "safe space," demonstrating that slower dissolution in a virtual batch would not negatively impact clinical performance, providing a science-based regulatory basis for dissolution specifications. In the second case study, PBBM explained the atypical food effect of omaveloxolone, a highly lipophilic amorphous formulation showing an approximate 350% increase in C_{max} but only 15% increase in AUC following a high-fat meal, a phenomenon driven by enhanced bile salt solubilization increasing absorption in the upper small intestine where first-pass metabolism is highest, causing a transient Cmax surge without a proportional AUC increase (*12*). In both cases, PBBM provided mechanistic insights that in vitro data alone could not capture, demonstrating its power as a tool for informed formulation design, food effect interpretation, and robust regulatory decision-making.

Dr. David Turner (on behalf of Dr Divyen Shah) demonstrated the development and validation of physiologically based pharmacokinetic (PBPK) models for mesalamine, a locally acting treatment for mild-to-moderate ulcerative colitis, using the Simcyp population-based PBPK simulator (V24). Given mesalamine's low systemic bioavailability (15–30%) and high population variability, model development began with an intravenous bolus model to establish systemic disposition, incorporating extensive N-acetylation. The model was subsequently extended to oral dosing with mechanistic determinants including colonic degradation, pH-dependent solubility, regional intestinal permeability via the MechPeff model, and a segregated transit time model for GI transit dynamics (*13*). Three marketed formulations (Pentasa, Apriso, and Lialda) were incorporated using dissolution data generated at the University of Florida as direct inputs, with pH-triggered release functions applied for enteric-coated formulations. Simulated plasma concentration-time profiles showed good agreement with clinical data across intravenous and oral dosing studies, and predicted luminal and colon enterocyte concentrations were broadly consistent with available literature values (*14*). The work highlights that plasma PK alone is insufficient to reflect therapeutic performance for locally acting drugs, and it demonstrates the model's suitability for virtual bioequivalence analysis and safe space assessments for locally acting drug products. This work was supported by FDA Grant U01FD007662 in collaboration with the University of Florida.

KEYNOTE SESSION

Recent advances in biopharmaceutics have substantially reduced reliance on animal studies through improved in vitro methods, deeper mechanistic understanding of formulation performance, sophisticated in silico modeling, and more efficient human study designs. Despite this progress, animal models continue to provide value when they are mechanistically relevant, when in vitro–in vivo translation is not established, or when integrated into model-informed development strategies. This keynote presentation by Dr. Sperry reviewed five case studies highlighting both the strengths and limitations of animal studies. In one example, distal intestinal delivery of an oral peptide with a permeation enhancer showed markedly higher bioavailability in dogs compared with proximal delivery, but the translation to humans is questionable. Other cases demonstrated limited predictive value of dog studies for certain formulations, though PBBM often provided useful directional insight. In contrast, successful integration of in vitro dissolution with PBBM accurately predicted food and proton-pump inhibitor effects for a poorly soluble BCS Class II compound. In situations where in vitro and in silico tools yielded ambiguous results, targeted rat and dog studies helped resolve solid form selection challenges. Species-dependent translation remains a key limitation. While dog models are well established, pig and minipig models show promise due to physiological similarities to humans, with published examples demonstrating strong concordance in drug exposure and tolerability (*14, 15*). Advanced in vitro systems and predictive in silico approaches are increasingly central to formulation development, provided model uncertainty is explicitly considered. Innovative, integrated CMC–clinical studies further enable real-time formulation optimization using human pharmacokinetic data (*16*). Overall, the optimal development strategy combines mechanistic insight, advanced in vitro and in silico tools, and judicious use of animal studies to support efficient pharmaceutical development.

CONCLUSION

Taken together, presenters across industry and academia suggest practical takeaways for future scientists developing pharmaceutical drug products. First, they underscore the value of mechanistic thinking in understanding how formulation properties, GI physiology (including enzymes and food effects), and dosage-form design interact to influence bioperformance, rather than relying solely on empirical dissolution tests. Second, they show that combining advanced in vitro systems with in

silico tools can meaningfully improve absorption and exposure predictions, support better decision-making, and reduce late-stage risk. Third, the talks highlight how computational dissolution analysis can be tailored to specific technologies (e.g., ASDs, orodispersible tablets) to guide formulation optimization and clinically relevant specifications. Finally, speakers emphasize that animal models remain valuable when mechanistically relevant, when in vitro translation is uncertain, or when integrated into model-based development. Overall, these presentations underscored the importance of integrating biorelevant experiments, preclinical and clinical studies, and modeling and simulation early and iteratively to streamline and de-risk drug development.

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The *AAPS Journal* High Impact Article Award: Challenges and Strategies for Solubility Measurements and Dissolution Method Development for Amorphous Solid Dispersion Formulations

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At the American Association of Pharmaceutical Scientists (AAPS) 360 PharmSci meeting held in San Antonio in November 2025, the article titled "Challenges and Strategies for Solubility Measurements and Dissolution Method Development for Amorphous Solid Dispersion Formulations," received the *AAPS Journal* High Impact Article Award (*1*). The authors of this timely and useful white paper are Drs. Andre Hermans, Johanna Milsmann, Hanlin Li, Christian Jede, Andrea Moir, Bart Hens, James Morgado, Tian Wu, and Michael Cohen. All are members of the International Consortium for Innovation and Quality in Pharmaceutical Development. The lead author, Dr. Andre Hermans, received the award in the 2025 AAPS High Impact Manuscript Award Rapid Fire session on Tuesday, November 11, 2025. He presented a summary of the paper from the podium. Dr. Hermans is a long-standing member of the In Vitro Release and Dissolution Testing (IVRDT) Community of the AAPS.

This award-winning white paper is extremely timely for the dissolution scientist, providing guidance for developing meaningful and appropriate methods for amorphous solid dispersion (ASD) formulations, which are challenging dosage forms that are becoming more common. A summary of the publication is provided below.

ARTICLE SUMMARY

This manuscript represents the view of the Dissolution Working Group from the Innovation and Quality Consortium on the challenges of and recommendations on solubility measurements as well as the development of dissolution methods for immediate release (IR) solid oral dosage forms formulated with ASDs. Nowadays, numerous compounds populate the industrial pipeline as promising drug candidates, yet they suffer from low aqueous solubility. In the oral drug product development process, solubility along with permeability is a key determinant to assure sufficient drug absorption along the intestinal tract. Formulating the drug candidate as an ASD is one potential option to address this issue. These formulations demonstrate the rapid onset of drug dissolution and can achieve supersaturated concentrations, which poses significant challenges to appropriately characterize solubility and develop quality control (QC) dissolution methods. Because ASD formulations have evolved during the last few years, there is no standard practice within the industry on how to assess drug solubility that is representative of such formulations. To address this gap, the authors summarized various methodologies to determine drug concentration for the intended purpose. The authors characterized the challenges for ASDs associated with (i) definition of solubility and sink conditions for ASD dissolution, (ii) applications and development of non-sink dissolution (according to conventional definition) for ASD formulation screening and QC method development, and (iii) advantages and disadvantages of using dissolution in detecting crystallinity in ASD formulations. Related to these challenges, successful examples of dissolution experiments in the context of control strategies were shared. The authors conclude that classical sink considerations are based on crystalline (thermodynamic, i.e., ≥ 24 h) drug solubility. Thus, they are only partly adequate for QC dissolution testing of

supersaturating ASD formulations. Instead, assessing the supersaturation concentration of the amorphous form allows the identification of the kinetic sink factor for such formulations. Given the inherent instability of supersaturated systems, harmonization of in vitro protocols to determine amorphous apparent drug solubility in ASD formulations would substantially increase the reliability and reproducibility of such measurements.

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Remembering Franz J. Fähler, Industry Trailblazer: A Personal Account

Franz J. Fähler, Founder of Pharma Test
(December 16, 1948–February 8, 2026)

We first met at a disastrous trade show in London in 1980. I felt a bit bad for this guy who had driven from Germany with a raft of equipment. I had never encountered dissolution before, so this was all quite novel. As I had done a PhD in pharmaceutical chemistry, this was something that I knew would be of interest. In the end, because of various jokes and innuendos, we were both laughing so hard that we had to sit down. We had an instant connection.

Franz founded Pharma Test in 1979 in an attic office in Hainburg, near Offenbach am Main, Germany. Through his previous sales experience in the drug quality control testing industry, he recognized the potential in this growing market. His goal was to set a new standard for testing quality-relevant properties of pharmaceutical products. Franz served as CEO until 2011, when his son, Björn, took over.

If you look at the older instrumentation and what we can offer now, you will see the influence of a keen and perceptive mind, producing instruments that are user-friendly and based on actual requirements, but with a view to future compendial directives.

We shared a lot of traits. A problem was simply a challenge waiting to be solved. “Never seen that before: a good time to learn something new! Every day is for learning,” he would say. I always liked his hands-on approach to new product ideas, and we made many road trips to customers, new production facilities and universities, continuously looking for new ways to achieve goals as well as employing totally innovative ideas and hardware. His dedication to customer happiness was second to none. Franz worked weekends and all the hours, and the results are clear: a firm foundation in thinking and practicality that is Pharma Test today.

On a personal note: Well, my friend, I will miss your company, the jokes, the laughs, and the beers. I was and am proud to call you, my friend. I know that I am not alone.

Dr. John Burmicz, Managing Director, Pharma Test Ltd, UK

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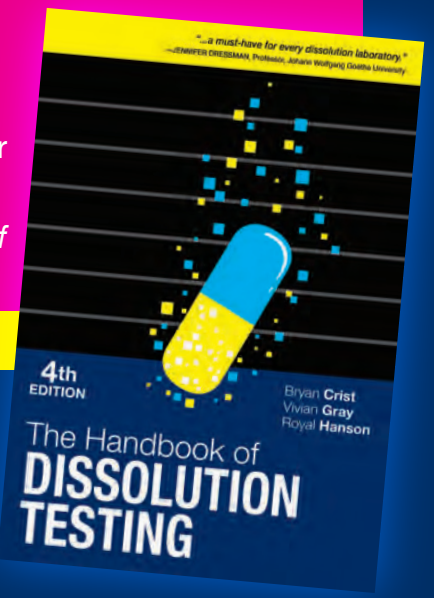

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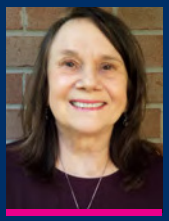

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Q+A Question & Answer Section

*The following questions have been submitted by readers of Dissolution Technologies. Margareth R. Marques, Ph.D. and Mark Liddell, Ph.D., United States Pharmacopeia (USP), authored responses to each of the questions. *Note: These are opinions and interpretations of the authors and are not necessarily the official viewpoints of the USP. E-mail for correspondence: mrm@usp.org.*

Q Regarding the use of USP apparatus 5, paddle over disk, for the drug release testing of transdermal systems, we are using 500 mL of dissolution medium. Figure 1b in the USP general chapter <724> Drug release shows the use of four clips to hold the screen and the watch glass. If we use the four clips, then the watch glass is going to be too high in the vessel, and with 500 mL of medium, it is going to be difficult to sample at the appropriate position, as described in the chapter. By removing one or two clips the watch glass will sit lower, and it will allow us to withdraw the samples as required. We would like to know if this new condition is acceptable.

A As stated in the chapter "other appropriate devices may be used, provided they do not sorb, react with, or interfere with the specimen being tested." Thus, it is not mandatory to use four clips as described in the chapter; any other suitable configuration can be used as long as the transdermal system and holder remain stable at the bottom of the vessel and do not move during the test.

Q We would like to know the allowed variability on the rotation speed in the dissolution test.

A See USP general chapter <711> Dissolution. For USP apparatus 1 (basket) and apparatus 2 (paddle), the tolerance is within ± 4% of the stirring rate specified in the method.

Q Are there any specific performance qualification tests that need to be done on the disintegration apparatus outside of what is performed in the Installation Qualification/ Operation Qualification?

A The disintegration equipment should meet the specifications for the measurements, materials, and assembly, as stated in the USP general chapter <701> Disintegration. Regarding the instrument performance, the stroke rate and stroke distance should be confirmed as part of the instrument qualification. From a day-to-day operational standpoint, the fluid surface height at the bottom and top of the stroke should be confirmed such that the wire mesh remains at least 15 mm below the surface of the fluid at the highest point of the upward stroke and descends to no less than 25 mm from the bottom of the vessel on the downward stroke. The operator should also confirm that the top of the basket-rack assembly does not become submerged at any point.

Q The USP general chapter <701> Disintegration states that the immersion fluid is to be kept at 37 ± 2 °C. Is there a requirement for the temperature of the water bath bar?

A No. The temperature of the water bath should be set to a temperature such that it maintains the temperature of the immersion fluid at 37 ± 2 °C throughout the entire duration of the test.

Q The dissolution acceptance criteria for a particular product is not less than (NLT) 80% (Q) of the labeled amount of drug substance is dissolved. If one unit has a result of 114% but the average of six results is 100%, would this result be valid?

A The dissolution results for immediate release dosage forms are evaluated using the Acceptance Table 1 in the USP general chapter <711> Dissolution (reprinted with permission from USP):

Acceptance Table 1

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit is Q + 5%.
S_2	6	Average of 12 units ($S_1 + S_2$) is ≥ Q, and no unit is < Q − 15%.
S_3	12	Average of 24 units ($S_1 + S_2 + S_3$) is ≥ Q, NMT 2 units are < Q − 15%, and no unit is < Q − 25%.

As can be seen in the table above, at stage S_1, each unit is NLT Q. In your example, each unit is NLT 80% + 5% of the product label claim, resulting in 85%. There is no calculation of the average amount released. Although the example provided, i.e., one individual result of 114%, would meet the requirements of the acceptance table, results above 100% should be investigated especially when the individual results are likely well outside of acceptable tablet assay limits. Possible reasons for results above 100% could be inappropriate filter used at the filtering step, interference of excipients or other components of the

dissolution test, inappropriate sampling technique, amongst many other possible sources. A root cause analysis would need to be performed to understand the source of the high results.

Q Is the amount of drug released at infinity point in dissolution comparable to the assay result, such that it can be compared to content uniformity?

A Infinity point (i.e., after collecting the sample at the last time point in the dissolution profile, the rotation speed is increased and the test is run for an extended period of time to extract as much drug substance as possible) is used to have an idea of the maximal amount of drug that may be released from the dosage form under extended dissolution conditions. It does not always have a direct correlation to the assay results because assay and uniformity of dosage unit samples are typically prepared using different methods. The infinity point can give you the total amount of drug released from each unit individually, but it represents the amount of drug released under dissolution conditions only.

Q Can the amount of drug obtained at the infinity point in dissolution testing be a replacement for the content uniformity test?

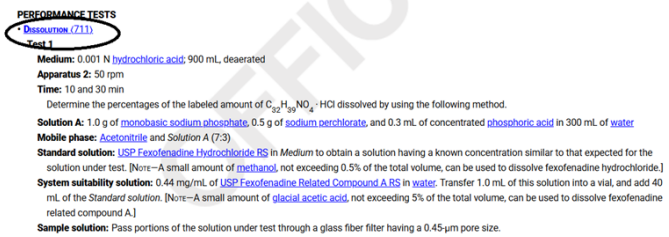
A As discussed above, the infinity point is not typically used in routine analysis. Normally, the infinity point is used during method development or formulation assessment to provide an understanding of the total amount of drug present and released from the sample under specific dissolution conditions. In addition, the sample is prepared using a different method for a content uniformity test. A content uniformity sample will typically be prepared using test conditions and methods like those used in the assay test.

Q Is it necessary to adjust the level of water in the dissolution equipment bath when using volumes of dissolution medium such as 500 or 250 mL.

A The recommendation is to keep the level of water in the bath above the level of dissolution medium in each vessel to keep the temperature of the dissolution medium at the temperature stated in the dissolution procedure. Whether it is necessary to adjust the level of water in the dissolution bath may depend on the mechanism used to secure the dissolution vessels to the vessel plate. In some cases, when the level of dissolution medium in the vessel is below the water level of the bath, the vessels may float and become unstable. It is best to adjust the water level in the bath high enough to maintain the temperature throughout the test, and low enough to ensure that the vessels are secure during the entire test.

Q Can apex vessels be used during the implementation of a dissolution test when there is no specific recommendation to use any vessel in a specific USP monograph? For example, can apex vessel be used in the dissolution tests in the USP monographs for Ciprofloxacin hydrochloride tablets and Fexofenadine hydrochloride tablets, as the monograph does not specify the type of vessel?

A Each USP monograph that has a dissolution test has the entry shown below:



PERFORMANCE TESTS

• Dissolution ⟨711⟩

Test 1

Medium: 0.001 N hydrochloric acid; 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 10 and 30 min

Determine the percentages of the labeled amount of $C_{32}H_{39}NO_4 \cdot HCl$ dissolved by using the following method.

Solution A: 1.0 g of monobasic sodium phosphate, 0.5 g of sodium perchlorate, and 0.3 mL of concentrated phosphoric acid in 300 mL of water

Mobile phase: Acetonitrile and *Solution A* (7:3)

Standard solution: USP Fexofenadine Hydrochloride RS in *Medium* to obtain a solution having a known concentration similar to that expected for the solution under test. [NOTE—A small amount of methanol, not exceeding 0.5% of the total volume, can be used to dissolve fexofenadine hydrochloride.]

System suitability solution: 0.44 mg/mL of USP Fexofenadine Related Compound A RS in water. Transfer 1.0 mL of this solution into a vial, and add 40 mL of the *Standard solution*. [NOTE—A small amount of glacial acetic acid, not exceeding 5% of the total volume, can be used to dissolve fexofenadine related compound A.]

Sample solution: Pass portions of the solution under test through a glass fiber filter having a 0.45-µm pore size.

The reference to Dissolution <711> is an indication that all the dissolution test conditions are consistent with those stated in <711> Dissolution. If the product was approved with conditions that differ from those stated in <711>, the specific conditions should be described in the monograph. Consequently, if the monograph does not specify any vessel, it means that the default vessel to be used is the one described in <711>. While there have been efforts to standardize the specifications for apex vessels, currently they are not standardized or described in any pharmacopeia. Therefore, like any noncompendial test method, they can only be used with appropriate scientific justification.

Q Regarding the use of pancreatin in a dissolution medium, in the "Determining Solubility and Stability of Drug Substance in Various Media" section of <1092> The Dissolution Procedure: Development and Validation, it is indicated that simulated intestinal fluid could be used as a typical medium. Could this medium be used in a product where cross-linking due to the gelatin coating is evident, or in what cases could it be used? Also, compared to <711>, there is a significant difference in the amount of pancreatin added to the medium.

A The conditions for the dissolution testing when there is evidence of the presence of cross-linking in gelatin capsules is described in the general chapter <711> Dissolution. The selection of the specific medium will depend on the solubility of the drug molecule. Further, the selection of an appropriate enzyme to be used to overcome the effects of cross-linking will depend on the pH of the dissolution medium. More information is in chapter <1094> Capsules - dissolution testing and Related Quality Attributes.

The preparation instructions for simulated intestinal fluid provided in the Test Solutions and Indicator Solutions section of the USP-NF are general instructions and use grams of

pancreatin powder, whereas in <711> Dissolution, the amount of pancreatin powder is expressed in units/L of dissolution medium. The actual amount of pancreatin powder, in grams, that one needs to add to the dissolution medium will depend on the activity of the specific lot of pancreatin.

Q In a scenario where a test is conducted with six tablets, and an equipment malfunction occurs—such as a failure to collect a sample from one vessel at a specific time point, or any other clearly identifiable equipment-related issue affecting a single vessel—would it be acceptable to repeat the test using one additional tablet and combine its results with the five valid results from the initial run?

A There are no official recommendations for such a situation, but it would be appropriate to consider the entire run invalid, document everything, and start the test again with six new units. The rationale for this approach is that the dissolution experiment with six tablets is intended for a single run with all tablets tested on the same equipment, by the same analyst. Running an additional run for the single failed tablet introduces an additional source of variability, specifically, run-to-run variability. Ultimately, the scenario should be discussed and evaluated internally, and discussions should include the quality assurance group.

Every issue of *Dissolution Technologies* features a Question and Answer section. This section is designed to address general dissolution questions submitted by our readers.

Please send your questions to:
Attn: Q&A
9 Yorkridge Trail, Hockessin, DE 19707
Email: vagray@rcn.com
Submit via our website:
www.dissolutiontech.com

Calendar of Events

June 11, 2026
Dissolution Testing - Ask us anything
Location: DDG Online Meeting at 10:30 am ET
Registration: https://www.agilent.com/chem/dissolution-webinars

June 16–17, 2026
Fundamentals of Dissolution: Guidance for the Verification and Qualification of a Dissolution Apparatus (Classroom/Laboratory)
Location: Milton Park, Oxfordshire (UK)
For information, visit https://lnkd.in/eHmkn79A

June 16–17, 2026
DissoAmerica 2026
Location: The Palace at Somerset Park in Somerset, NJ, USA
For information, visit SPDS.us

July 6–9, 2026
Controlled Release Society 2026 Annual Meeting
Location: Lisbon, Portugal
Registration: https://www.edgereg.net/er/Registration/StepRegInfo.jsp?ActivityID=43871

October 7–8, 2026
INSIGHT 2026 Pharmaceutical Conference
Location: Dublin, Ireland
For information, visit www.insight2026.com

October 25–28, 2026
PharmSci 360 AAPS Meeting
Location: Ernest N. Morial Convention Center, New Orleans, LA
For information, visit https://www.aaps.org/pharmsci/annual-meeting

November 5, 2026
Let's talk - From Dissolution Sample Preparation to LC Finish
Location: DDG Online Meeting at 10:30 am ET
Registration: https://www.agilent.com/chem/dissolution-webinars

November 16–18, 2026
Eastern Analytical Symposium and Exhibition
Location: Crowne Plaza Princeton-Conference Center, Plainsboro, NJ, USA
For information, visit eas.org

December 1–2, 2026
Long-Acting Injectable (LAI) Generics: Navigating Technical Hurdles in Product Development and Regulatory Assessment
Location: Universities at Shady Grove, Rockville, MD
Registration: https://www.complexgenerics.org/education-training/long-acting-injectable-lai-generics-navigating-technical-hurdles-in-product-development-and-regulatory-assessment/

On Demand Events

- ***Powder Flow Testing***
  https://www.copleyscientific.com/events/webinar-foundations-of-powder-flow-testing/
- ***dissoLab Software: Predictive Dissolution Simulated from Microscopic Images***
  https://vimeo.com/1054617734?share=copy
- ***Fiber Optic UV: Better Dissolution Testing On Demand***
  https://www.distekinc.com/watch/fiber-optic-uv-better-dissolution-testing/

- ***Advances in In Vitro Bioequivalence Assessment for Topical Products Part 2***
https://youtu.be/iqphypToHZ0?si=mn9FJLDhm-VBoWMm

- ***Ocular Administration (OCAT™) in GastroPlus® On Demand***
https://www.simulations-plus.com/events/gastroplus-additional-dosage-routes-workshop-ocular-administration-ocat-virtual/

- ***Oral Cavity Administration (OCCAT™) in GastroPlus® On Demand***
https://www.simulations-plus.com/events/gastroplus-additional-dosage-routes-workshop-oral-cavity-administration-occat-virtual/

- ***Pulmonary Administration (PCAT™) in GastroPlus® On Demand***
https://www.simulations-plus.com/events/gastroplus-additional-dosage-routes-workshop-pulmonary-administration-pcat-virtual/

- ***GastroPlus® ADR – 4 Course Bundle (TCAT™ / OCAT™ / OCCAT™ / PCAT™)***
https://www.simulations-plus.com/events/gastroplus-adr-4-course-bundle-tcat-ocat-occat-pcat/

- ***GastroPlus® ADR – 5 Course Bundle (TCAT™ / OCAT™ / OCCAT™ / PCAT™ / Injectables)***
https://www.simulations-plus.com/events/gastroplus-adr-5-course-bundle-tcat-ocat-occat-pcat-injectables/

- ***Transdermal Administration (TCAT™) in GastroPlus®***
https://www.simulations-plus.com/events/gastroplus-additional-dosage-routes-workshop-transdermal-administration-tcat-virtual/

- ***Injectables (IM, SQ, IA) in GastroPlus® Including Biologics and LAIs***
https://www.simulations-plus.com/events/gastroplus-additional-dosage-routes-workshop-injectables-incl-lai-biologics-virtual/

- ***GastroPlus® X Tutorial Series***
https://www.simulations-plus.com/events/gastroplus-x-tutorial-series/

- ***GastroPlus® X Tutorial Series I – Panels and Start-up Essentials***
https://www.simulations-plus.com/courses/gastroplus-x-tutorial-series1/

- ***GastroPlus® X Tutorial Series II – Modules***
https://www.simulations-plus.com/courses/gastroplus-x-tutorial-series-ii-modules/

- ***GastroPlus® X Tutorial Series III – New Features in GastroPlus X.2***
https://www.simulations-plus.com/courses/gastroplus-x-tutorial-series-iii-new-features-in-gastroplus-x-2/

- ***Complimentary Introduction to GastroPlus® for up to v.9.9***
https://www.simulations-plus.com/events/complimentary-introduction-to-gastroplus-v-9-9/

- ***Complimentary Introduction to GPX™***
https://www.simulations-plus.com/events/complimentary-introduction-to-gpx/

Free Tutorials (AI Language Translation)

- ***GastroPlus® Tutorial in French***
https://www.youtube.com/watch?v=h-_4m8xpDg8&list=PLQuCii74Pfd327VslFvlp_lRxqJlfzEF0

- ***GastroPlus® Tutorial in Japanese***
https://www.youtube.com/watch?v=IkTsLRPVIms&list=PLQuCii74Pfd317she0RsVTFVCyI2yvz9X

- ***GastroPlus® Tutorial in Mandarin***
https://www.youtube.com/watch?v=XabV2jiAsVU&list=PLQuCii74Pfd3LojzBlatK7mnbLxPvqFDa

- ***GastroPlus® Tutorial in Portuguese***
https://www.youtube.com/watch?v=idkaPR6av9M&list=PLQuCii74Pfd0zttMQdhy6sv97OlK9MyE5

- ***GastroPlus® Tutorial in Spanish***
https://www.youtube.com/watch?v=kEmj98nnpx8&list=PLQuCii74Pfd2oVl6tsQNvxZs6sX0Ww9FT

Industry News

Distek Introduces the OLERA Dissolution Instrument Series

The New Standard In Dissolution Testing, Bringing the Latest in Instrumentation Features

North Brunswick, NJ - Distek, Inc., a leading manufacturer of dissolution instrumentation for 50 years, announced the release of the **OLERA Dissolution Instrument Series**, a new platform engineered to enhance dissolution testing through an improved user experience based on simplified operation and modern system connectivity.

The OLERA Series includes three models—**OLERA, OLERA Plus, and OLERA Select**—designed to address the requirements of the modern pharmaceutical laboratory at all price-performance levels while preserving the reliability and longevity associated with Distek systems.

Designed for Today's Laboratory Environment

The OLERA Series supports **USP Apparatus 1, 2, 5, and 6**, along with intrinsic, immersion, and small volume dissolution methods, providing flexibility across a wide range of applications.

All models incorporate a large touchscreen interface, advanced vessel alignment, and optional remote monitoring through **Pulse**, enabling browser-based system access and automated notifications without additional software.

Three Configurations Aligned to Laboratory Needs

- **OLERA** – A traditional bath-based dissolution instrument with integrated heating and circulation, reducing system complexity and external components, priced to compete with any other dissolution system available.
- **OLERA Plus** – Extends the OLERA platform with patented in-shaft temperature monitoring, enabling continuous, real-time temperature measurement for complete compliance assurance throughout the run.
- **OLERA Select** – A bathless dissolution instrument utilizing proprietary heating technology to eliminate the water bath, resulting in rapid media heating, reduced energy use by up to 40%, and operation up to 99 °C.

DISTEK

Core Technologies Across the Platform

- **Patented In-Vessel Temperature Monitoring (OLERA Plus & Select)** provides continuous temperature recording without fragile sensors impacting vessel hydrodynamics.
- **Integrated Heating & Circulation (OLERA & Plus)** delivers space-saving built-in thermal controls without external heater/circulators.
- **Bathless Heating (OLERA Select)** eliminates the water bath and attendant cleaning, reduces warmup time and energy use.
- **Large Touchscreen Interface** features a 10-inch display for a superior UI experience and simplified operation.
- **acculign+ Automated Vessel Alignment** ensures reproducible mechanical alignment from run to run.
- **HALO Status Indicator** provides at-a-glance system status.
- **Pulse Remote Monitoring** enables browser-based monitoring with text and email alerts.
- **FLEX Low Temperature** supports testing down to 5 °C with an external chiller.

Learn More

Live and virtual demonstrations of the OLERA dissolution instruments are available. To learn more or schedule a demonstration, contact sales@distekinc.com or visit www.distekinc.com.

Distek is proud to celebrate 50 years of supporting pharmaceutical laboratories worldwide.

About Distek

Distek, Inc. designs and manufactures innovative pharmaceutical laboratory instrumentation used in research, development, and quality control laboratories worldwide. The company specializes in dissolution testing systems and supporting technologies recognized for their reliability, precision, and customer-focused design. For 50 years, Distek has supported pharmaceutical laboratories with solutions that improve performance, streamline workflows, and ensure consistent, high-quality results.

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121 North Center Drive
North Brunswick, NJ 08902
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Building the Fully Automated Dissolution Lab: Architecture, Integration Strategy, and Return on Investment in Modern QC and R&D Environments

By Martin Kühn and David Kötterheinrich, ERWEKA, Langen, Germany

In pharmaceutical quality control and research laboratories, dissolution testing remains one of the most critical, and closely regulated, analytical processes. It determines how a drug product releases its active pharmaceutical ingredient under defined conditions, directly influencing batch release decisions, regulatory compliance, and ultimately patient safety.

Although production environments have embraced high levels of automation, many dissolution labs still operate with partially manual workflows. Sampling by hand, paper-based documentation, shift handovers, and fragmented data systems introduce variability, delay, and risk. As cost pressures increase and regulatory scrutiny intensifies, laboratories are reexamining what a fully automated dissolution lab actually means in practical terms, and how to move toward that goal in a realistic, phased way.

A fully automated dissolution lab is an integrated, end-to-end architecture that enables reproducible testing, continuous throughput, and reliable data integrity. Understanding its building blocks, and how they function together, is the first step toward designing a future ready laboratory.

The Core Architecture of an Automated Dissolution Environment

A dissolution workflow involves far more than immersing tablets in media. A complete cycle typically includes apparatus setup, media preparation, sample loading, timed sampling, potential secondary filtration, transfer to analytical instrumentation, and cleaning in preparation for the next batch. In a traditional laboratory configuration, many of these stages are handled independently. The dissolution bath operates as one unit, samples are manually collected and transferred, analytical testing occurs on a separate instrument, and documentation is recorded either on paper or in disconnected systems. Though compliant, this approach creates multiple handoff points, each one a potential source of delay, inconsistency, or transcription error.

ERWEKA'S automated dissolution system delivers precise robotic sampling and consistent unattended operation.

In an automated environment, these elements are architected to function as a coordinated system rather than isolated instruments. The dissolution tester, automated sampling module, fraction collector or direct injection interface, and UV–Vis or high-performance liquid chromatography (HPLC) system are integrated through centralized control software. Timed sampling is synchronized precisely with analytical measurement. Temperature, paddle speed, and sampling intervals are recorded automatically. Data generated during dissolution flow directly into analytical platforms and is compiled into structured batch reports.

Higher levels of automation extend this integration further, enabling robotic platforms to manage the full sequence from vessel preparation through cleaning and readiness for the next run. Instead of operators moving physically between instruments, the workflow progresses seamlessly within a single connected architecture. The result is not simply faster testing, but a unified system that improves repeatability, reduces manual intervention, and strengthens overall process control.

From Manual Testing to "Lights Out" Operation

In its most advanced form, a fully automated dissolution lab operates with minimal human intervention. Analysts prepare methods and load samples, initiate the run, and the system performs the repetitive, time sensitive tasks automatically, often overnight or across weekends. The concept is sometimes referred to as a "lights out lab," where the equipment continues executing validated workflows while personnel focus on higher value analytical or research activities.

The motivation is not simply labor reduction. In fact, many pharmaceutical laboratories cite skilled labor shortages and increasing documentation demands as primary drivers of automation. Furthermore, dissolution runs frequently extend beyond a single operator's shift. When one analyst starts a 12-hour run and another finishes it, handovers introduce documentation burden and the potential for deviation. Manual sampling techniques, such as withdrawing aliquots with a cannula and syringe, can vary subtly based on operator speed, positioning, or technique, influencing reproducibility.

If unexpected results occur at the end of a long run, the consequences are significant. A batch may be placed on hold, investigations initiated, and retesting required, consuming additional time and capital. Automated systems execute sampling and timing identically, every time, reducing this variability and strengthening reproducibility. In this sense, automation is as much about risk mitigation and consistency as it is about speed.

One of the most important strategic insights for laboratories is that full automation is rarely an overnight transformation. Transitioning directly from manual sampling to a fully robotic solution can disrupt workflows, training requirements, and operational culture. A more sustainable approach is phased automation. Laboratories often begin with standalone dissolution testers, then add automated sampling modules, followed by offline or online integration with UV–Vis or HPLC systems. Over time, these systems can be upgraded further with additional pumps, fraction collectors, and enhanced software modules, protecting the initial investment while increasing capability.

This scalability ensures that automation aligns with evolving throughput demands and budget realities. Importantly, future proof system architecture allows laboratories to expand without replacing foundational equipment.

Throughput, Reproducibility, and ROI

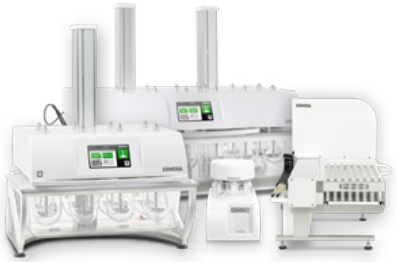
Automation's financial case rests on both tangible and intangible factors. From a throughput perspective, automated systems enable 24/7 operation. In many organizations, tablet production is highly automated and continuous, yet quality control remains a bottleneck. Accelerated testing and batch release allow finished products to reach market sooner, improving cash flow and freeing working capital. Return on investment calculations typically compare current labor hours, retesting frequency, documentation time, and equipment utilization against projected automated workflows. Although utilization rates vary, many laboratories observe payback periods of less than 2 years, depending on volume and operational structure.

Equally significant is reproducibility. Common operator errors in dissolution testing include inconsistent media preparation, sampling outside defined time windows, or technique related variability. Automation standardizes these steps, reducing the likelihood of deviations that could trigger investigations or delayed batch release. Although the cost of an error is difficult to quantify precisely, the downstream impact of failed releases, regulatory findings, or repeated analyses often exceeds incremental labor savings.

Integration in Practice: Scalable Platforms for Modern Laboratories

As laboratories evaluate automation strategies, the ability to scale over time becomes a defining consideration. ERWEKA, a global manufacturer of pharmaceutical dissolution and tablet testing equipment, has structured

its portfolio around this principle of upgradeability and integration depth. At the foundational level, ERWEKA provides pharmacopeia compliant dissolution testers for widely used USP Apparatus 1 and 2 methods, while supporting the full USP 1 through 7 range for diverse dosage forms, including transdermal systems and specialized applications. This breadth allows laboratories to standardize across multiple product categories rather than relying on separate vendors.



ERWEKA's automated dissolution platform with integrated sampling and analytical connectivity, designed to support scalable lab automation.

As automation needs increase, ERWEKA systems can be configured to incorporate automated sampling, offline fraction collection, or online integration with UV–Vis and HPLC instrumentation. In advanced configurations, samples can be transferred directly into the analytical loop of an HPLC system, streamlining the workflow from dissolution to quantification. Because the same base platform can be expanded over time, laboratories are able to preserve initial capital investments while moving progressively toward higher levels of automation.

Beyond hardware integration, emphasis on intuitive software interfaces, robust audit trail functionality, and durable mechanical design contributes to ease of operation and long-term reliability. In a regulatory environment where core dissolution parameters are tightly defined by pharmacopeial standards, differentiation often lies not in extreme performance specifications but in usability, integration capability, and the ability to support a laboratory's full automation journey.

Preparing for the Next Decade of Dissolution Testing

Over the next 5–10 years, dissolution laboratories are expected to continue advancing toward two defining priorities: comprehensive automation and uncompromised data integrity.

The lights out lab, capable of continuous, unattended operation, represents a logical progression as labor constraints persist and production timelines accelerate. Simultaneously, seamless digital integration between instrumentation, analytical systems, and enterprise platforms will become standard rather than exceptional.

For quality control and R&D laboratories navigating cost pressure and regulatory complexity, the fully automated dissolution lab is no longer a distant ideal. It is an achievable, phased evolution, grounded in thoughtful system architecture, scalable integration strategy, and disciplined execution.

Simulations Plus Announces Strategic Collaboration Programs for AI-Enabled Modeling

Co-development initiatives to advance next-generation workflows, accelerate adoption, and expand the role of AI within model-informed drug development

Simulations Plus, Inc. (Nasdaq: SLP), a global leader in model-informed and artificial intelligence (AI)-accelerated drug development that advances biopharma innovation, announced strategic collaboration programs with three large pharmaceutical companies to advance AI workflows across the drug development lifecycle.

These programs apply AI within scientifically grounded modeling workflows and define how next-generation workflows are deployed at scale. The close collaboration between Simulations Plus and leading pharmaceutical organizations will provide direct insight into how AI will be integrated into real-world environments—informing product direction, workflow standardization, and future commercial models. The programs will utilize the Simulations Plus major software platforms, including GastroPlus®, MonolixSuite™, ADMET Predictor®, and Thales™.

"Our approach to AI is grounded in how it operates within a complete system, not as a standalone capability," said Jonathan Chauvin, Co-Chief Product & Technology Officer at Simulations Plus. "These collaborations will allow us to work alongside our partners, leveraging real-time scientific feedback and company data to continuously refine how workflows are orchestrated across our tools, ensuring AI-driven efficiencies translate into reproducible, traceable outcomes. The insights we gain will directly shape how we evolve our platform and deliver value at scale."

Participating companies will integrate the company's internally developed AI agents directly into model-informed drug development (MIDD) workflows, enabling natural language interaction, automation of data processing, coordination of simulations across multiple modeling engines, and generation of interpretable outputs from complex, multistep pipelines.

Importantly, the collaborations will also serve as a foundation for broader enterprise adoption, including direct alignment with information technology teams to define how AI-enabled capabilities are deployed, governed, and integrated within existing systems. This includes defining standards together for transparency, reproducibility, and governance as AI becomes more deeply embedded in drug development processes.

"As highlighted at our Investor Day presentation in January, AI will only fulfill its potential in drug development when it is delivered responsibly, grounded in validated science, and integrated into real workflows," said Shawn O'Connor, Chief Executive Officer of Simulations Plus. "Our customers are choosing to work with us because of the strength of our validated scientific engines and depth of our teams who apply them daily within real workflows, enabling us to translate AI into practical, deployable solutions. These strategic collaboration programs represent an important step in moving us and our partners beyond experimentation and into practical implementation as we advance our software and services into a unified modeling ecosystem."

Companies interested in learning about using AI-enabled workflows in their modeling can request additional information.

olera
DISSOLUTION PLATFORM

OLERA Select

Reliable Dissolution Testing, Reimagined

Advanced bathless technology.
Smart monitoring. Proven results.
Designed for modern laboratories.

LARGE 10" COLOR TOUCHSCREEN
Intuitive control, clear visibility, and easier operation.

IN-VESSEL TEMPERATURE MONITORING
Continuous, real-time temperature measurement with no hydrodynamic impact.

BATHLESS HEATING TECHNOLOGY
Eliminates the water bath and reduces energy use by up to 40%. Heats rapidly to 37 °C and up to 99 °C.

HALO STATUS INDICATOR
One glance confirms system status across the laboratory.

PULSE REMOTE MONITORING & ALERTS
Monitor status from any browser with optional email and text alerts.

OLERA Select redefines dissolution testing with advanced bathless heating technology, eliminating the water bath while reducing energy use by up to 40%. Built on Distek's 50 years of proven instrument design, it delivers efficient performance for laboratories seeking reliable results and lower operational costs.

SCAN TO LEARN MORE
Explore OLERA Select. Request a virtual or live demo and configure your next instrument.

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Agilent OpenLab

Unlock the Future of Laboratory Compliance

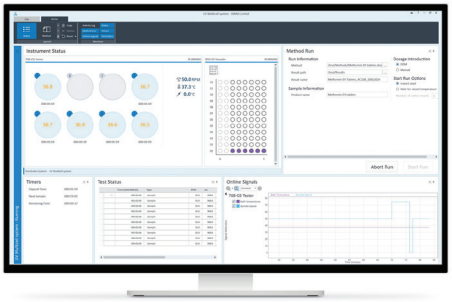
Dissolution is now on OpenLab

Introducing the Agilent Dissolution Workflow Manager for OpenLab CDS. Whether you're using Agilent OpenLab CDS, another dissolution software, or managing testing manually, Agilent has a solution for you. This software add-on for OpenLab CDS ensures superior data integrity and consolidates all your test results in one place.

Benefits at a glance:

- Secure data storage
- Enhanced compliance
- Improved user-friendly interface
- Minimized validation effort

Learn more at: www.agilent.com/dissolution/workflow-manager



Agilent
Trusted Answers

DE-008230