

## Intrinsic Dissolution

### Provided to Help You Get the Most from Your Agilent Dissolution Products!

Intrinsic dissolution rate is defined as the dissolution rate of a pure drug substance under the condition of constant surface area. Knowledge of the intrinsic dissolution properties of new drug candidates is vital to optimizing the physiological effectiveness on new dosage forms. During ANDA filing, drug substances must be evaluated to show consistent physical characterization as represented by its dissolution rate constant. For instance, drug substances with intrinsic rates of less than 0.1 mg/min/cm<sup>2</sup> will be dissolution rate limited whereas, drug substances with intrinsic rates of greater than 1 mg/min/cm<sup>2</sup> will most likely be free of dissolution rate problems.

Drug substances, available from multiple sources, must demonstrate uniformity in the manufacturing process and physio-chemical make-up of the drug substance. Parameters directly affecting the solubility of the drug substance depend on crystallinity, amorphism, polymorphism, hydration, solvation, particle size and overall particle surface area.

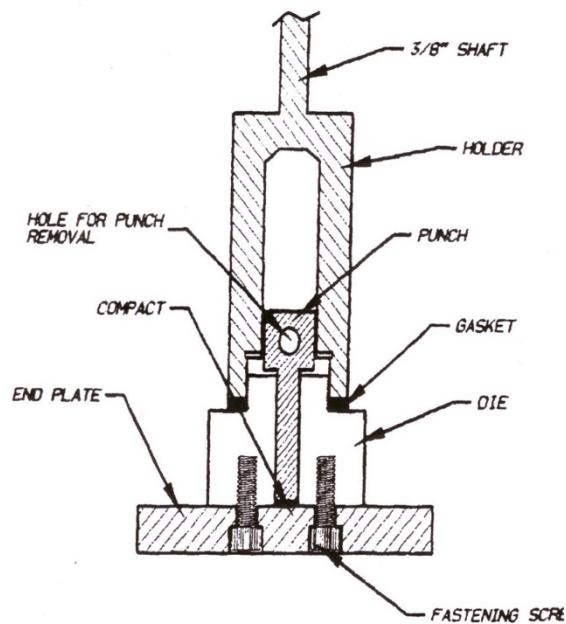
According to USP Chapter <1087> Apparent Intrinsic Dissolution

Dissolution rate generally is expressed as the mass of solute appearing in the dissolution medium per unit time (e.g., mass sec<sup>-1</sup>.) Reporting dissolution flux is preferred because it is normalized for surface area and, for a pure drug substance, is commonly called intrinsic dissolution rate.

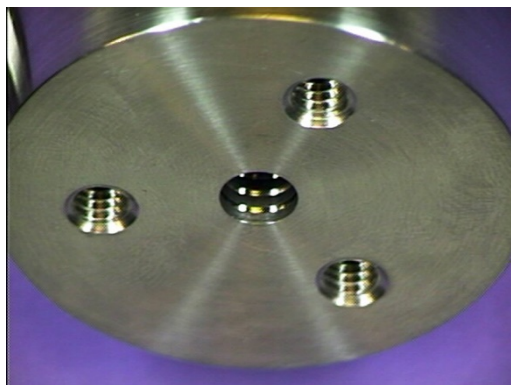
This is also known as the constant surface area method which utilizes a compressed disc of known area. This method eliminates surface area and surface electrical charges as dissolution variables. The dissolution rate obtained by this method is termed the intrinsic dissolution rate and is characteristic of each solid compound in a given solvent under the fixed experimental conditions.

### Technical details

Intrinsic dissolution is determined by compressing pure powdered drug substances using a specially constructed punch and die system under high pressure to obtain a nondisintegrating disk (pellet). This is performed without the addition of any excipient such as a binder or lubricant to avoid external interference in the intrinsic dissolution profile. The disk assembly is then transferred to a dissolution apparatus for determination of the rate of release.



The punch and die are constructed of hardened steel as well as the base which is polished mirror smooth for compacting the pellet. The die is typically 0.1 to 1.0 cm with a diameter cavity of 0.8 cm dia. = 0.5 cm<sup>2</sup>. The die utilizes a gasket to form a liquid seal from the dissolution media and is screwed into the shaft/holder assembly to mount into dissolution apparatus. The inner surface of the die cavity scored with ring indentions to retain compact drug substance within the die during the test. The die and the holder are constructed of 316 stainless steel.





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The Intrinsic Dissolution Apparatus provides the dissolution rate of a pure active pharmaceutical ingredient (API) by exposing the API with a constant surface area to the dissolution medium. The intrinsic rate is determined by rotating the apparatus in a dissolution vessel containing 37 °C media and pulling samples until at least 10% of the API has dissolved. The rate is then calculated by plotting the cumulative amount of API dissolved from the exposed surface area versus time.

### Intrinsic Dissolution Apparatus

Description	Part Number
Intrinsic Dissolution Apparatus, 0.5 cm <sup>2</sup> exposed surface area, with punch, shaft and holder, for 7000E/7010, 708-DS, 705-DS*	12-4101
Intrinsic Dissolution Apparatus, 0.125 cm <sup>2</sup> exposed surface area*	12-4110
Intrinsic die, 0.5 cm <sup>2</sup> exposed surface area	12-4120
Punch	12-4140
Shaft and die holder only, for intrinsic dissolution	12-4150
Surface plate, for intrinsic dissolution	12-4130

\*Surface plate sold separately. Only one plate required for testing.

Note: The Intrinsic Dissolution Apparatus is not recommended for use with DVH models, including the 7030 and the 709-DS.

### Intrinsic Dissolution Apparatus Example

In addition to the standard dissolution apparatus, to configure a 708-DS for intrinsic dissolution use, see the following example:

#### Intrinsic Dissolution Ordering Example: 708-DS, 6 positions

Quantity	Description	Part Number
6	Intrinsic Dissolution Apparatus, 0.5 cm <sup>2</sup> exposed surface area, with punch, shaft and holder, for 7000E/7010, 708-DS, 705-DS	12-4101
1	Surface plate, for intrinsic dissolution	12-4130

Literature/specification sheet

[http://intranet.chem.agilent.com/Library/datasheets/Public/5990-7402EN\\_Intrinsic%20Apparatus.pdf](http://intranet.chem.agilent.com/Library/datasheets/Public/5990-7402EN_Intrinsic%20Apparatus.pdf)



Link to video

[http://read.nxtbook.com/agilent/source\\_book/dissolution\\_systems\\_2017\\_2018/intrinsic\\_dissolution.html](http://read.nxtbook.com/agilent/source_book/dissolution_systems_2017_2018/intrinsic_dissolution.html)

Other information (PowerPoints, Webinars)

Dissolution Discussion Group Online Meeting (Recorded February 12, 2015 and requires WebEx Viewer): Method Development Considerations: Intrinsic Dissolution

[http://www.dissolution.com/2015\\_02\\_12.arf](http://www.dissolution.com/2015_02_12.arf)

## Agilent Sites and Services for Your Dissolution Workflow



Agilent Dissolution Systems Digital Source Book

[www.nxtbook.com/nxtbooks/agilent/dissolution\\_sourcebook/index.php](http://www.nxtbook.com/nxtbooks/agilent/dissolution_sourcebook/index.php)

Dissolution Exchange

[www.dissolution.chem.agilent.com](http://www.dissolution.chem.agilent.com)

Dissolution 1-on-1 Training

[www.dissolution.chem.agilent.com/learndissolution-1-on-1](http://www.dissolution.chem.agilent.com/learndissolution-1-on-1)

Dissolution Hotline (Email Address)

[dissolution.hotline@agilent.com](mailto:dissolution.hotline@agilent.com)

Dissolution Discussion Group (DDG)

[www.dissolution.com](http://www.dissolution.com)