

## Disintegration Test Interview Questions and Answers:

### What is Dissolution?

Dissolution is the process by which a solid substance becomes incorporated into a solvent to form a solution. In the field of pharmaceutical science, it means that before drugs are taken in by systemic circulation, before being absorbed into the systemic circulation. This is why dissolution rate and extent can impact on bioavailability of drugs and thus considered as critical quality attributes in development and approval of oral solid dosage forms.

### What is the Principle of Dissolution:

Dissolution is a test to identify the rate at which a drug dissolves into a given set of conditions such as Temperature, pH, stirring speed, etc.

### Why is Dissolution testing important in Pharmaceutical industry?

Dissolution testing is essential because it examines how fast a drug is released from its dosage form into the body which affects its bioavailability and efficacy. It also promotes uniformity in manufacturing batches of medicines which is important for patient safety purposes. For regulatory authorities, detailed data about dissolution testing must be available before new drugs are approved or existing ones go to market.

### What are the different types of Dissolution apparatus used for testing?

There are several types of dissolution apparatuses used in the pharmaceutical industry, each designed to mimic various conditions in the gastrointestinal tract. The USP describes at least seven different types of apparatus:

**Apparatus 1 (Basket type):** A rotating basket that holds the dosage form is used in a vessel filled with dissolution medium. It is suitable for capsules, tablets, and floating dosage forms.

**Apparatus 2 (Paddle type):** Consists of a paddle that stirs the dissolution medium in which the dosage form is immersed. It is widely used for tablets and capsules.

**Apparatus 3 (Reciprocating cylinder):** Offers the option to change the dissolution medium during the test, useful for extended-release products.

**Apparatus 4 (Flow-through cell):** A flow cell through which the dissolution medium flows and encompasses the dosage form, suitable for poorly soluble drugs.

**Apparatus 5 (Paddle over disk):** Used for transdermal patches, where a paddle moves over a stationary disk that holds the patch.

**Apparatus 6 (Cylinder):** It is mainly used For suppositories, it uses a cylinder instead of a basket or paddle.

**Apparatus 7 (Reciprocating holder):** Alternates for specific use cases, similar to apparatus 3 but uses a holder that moves up and down within the dissolution medium.

## **What is the Difference between Dissolution and Disintegration?**

Dissolution and disintegration are two distinct but important processes that are measured during pharmaceutical analysis. Disintegration refers to the physical break-down of a dosage form e.g. tablet or capsule into smaller fragments or granules, even without necessarily being dissolved completely. This happens before dissolution can take place. In contrast, actual drug substance dissolves in a solvent usually mimicking body fluids, to form a solution, making the active pharmaceutical ingredient available for absorption into the body. if talk about disintegration, This acts as a precursor to dissolution, it does not involve in the active drug's availability for absorption.

## **How does Particle size affect Dissolution rate?**

The rate of dissolution for a drug is significantly influenced by particle size in its formulation. Smaller particles have greater surface areas compared to larger ones; thus, they expose more of their surfaces with the solvent. The solvent works faster on this larger area which enhances its effectiveness at dissolving the active substance, resulting in a faster dissolution rate., Therefore, medicines having smaller particle sizes tend to have high bioavailability since absorption of

active ingredients occurs more easily in them. However, the exact relationship between particle size and dissolution rate can also depend on other formulation factors and the physicochemical properties of the drug substance.

### **Explain sink conditions in Dissolution testing.**

When the volume of a solvent in dissolution testing is large enough to ensure that the solution does not get saturated with solution, it is referred to as sink conditions. This is like ensuring there is always room for more sugar in a cup of tea, such that the sugar keeps dissolving instead of accumulating at the bottom-most part. It allows us to measure the rate of dissolution accurately without complications that could arise from recrystallization or incomplete solubility due to saturation.

### **What is Supersaturation and How it can be controlled during**

To answer this question we have to understand how sink conditions work. In simple words, supersaturation means that a solution may contain more dissolved material than it would under normal equilibrium conditions. If a drug's solubility exceeds its saturation point or if there are any changes in temperature or pH in the medium, then this could occur. In dissolution testing, sink conditions also avoid supersaturation.

### **What is the Purpose of Dissolution testing?**

The purpose of dissolution testing is to predict how the drug behaves in the human body, acting as a vital indicator of its bioavailability and therapeutic effectiveness. By mimicking the process of dissolving in the gastrointestinal tract, dissolution tests help determine the rate at which the active pharmaceutical ingredient is made available for absorption. This information is crucial for drug design, formulation optimization, and quality control, ensuring that each batch of medication released to the market meets the required standards to provide patients with consistent therapeutic outcomes.

### **What Factors Can Influence Drug Dissolution?**

Below are the Several factors that can influence the rate and extent of drug dissolution, which include:

**Drug Solubility:** For absorption to take place, the drug must dissolve in an aqueous solution. The slow dissolution of drugs with low solubilities results in poor bioavailability.

**Drug Formulation:** A rate of dissolution can be altered by tablet excipients, which are substances formulated with the active ingredient. For instance, disintegrants quicken it up while some polymers retard its progress.

**Medium pH:** The solubility of a drug may significantly depend on the pH of gastrointestinal fluids since they keep changing.

**Agitation and hydrodynamics:** By thinning the diffusion layer around a particle of drug, stirring speed and overall dynamics of dissolution medium improve the dissolution rate.

**Temperature:** The dissolution process can be improved by increasing temperature which generally leads to greater kinetic energy among molecules

**Particle Size and Area:** As noted earlier, smaller particle sizes with larger surface areas are more likely to dissolve.

**Polymorphism:** There are multiple crystalline forms that exist for drugs and each form exhibits different dissolution rates due to various molecular packings.

**Drug Stability:** Solubility as well as the dissolving rate for active pharmaceutical ingredients may change upon degradative product formation.

## **How is Media selection done for Dissolution studies?**

The selection of the medium for dissolution test is important to ensure similarity between the test results and physiological conditions in humans. It is a process that considers drug's chemical nature, solubility, and Gastrointestinal environment. Mostly, aqueous solutions like hydrochloric acid, phosphate buffer, and acetate buffer with a pH range of 1 up to 7.5 are used to mimic stomach and intestinal fluid flow.

Additionally, it must not react with either the drug or apparatus employed. On some occasions, surfactants are added into the medium in order to enhance solubility of drugs that are poorly soluble in water. The focus is on making sure that it dissolves at a rate representative of what it would be like if ingested hence giving valuable details on its bioavailability.

## **What is the Difference between USP Apparatus-1 and USP Apparatus-2?**

The USP Apparatus 1, also called the basket apparatus and USP Apparatus 2 known as the paddle apparatus are two commonly applied types of dissolution testing instruments though they operate differently. In this case, USP Apparatus 1 has a rotating basket that contains the sample which is in turn immersed in the dissolution medium and this is particularly suitable for capsules and floating dosage forms.

On the other hand, USP Apparatus 2 makes use of a paddle that mixes the dissolution medium above the sample while it remains stationary at the bottom of the vessel. It serves tablets best in most cases. Whether to use these two apparatuses will largely depend on what formulation of drug is being tested and whether it's a tablet or not. These two devices are designed to give reliable results that would reproduce actual drug release characteristics in the human body.

## **Can you explain the working principle of each USP apparatus used for Dissolution testing?**

The **USP Apparatus 1**, basket apparatus principle of operation depends on holding the dosage form inside a mesh wire basket which is then put in a dissolution medium. The basket rotates at a specified speed, making it possible for fluid to flow smoothly through the dosage form. The drug is dissolved and then dispersed throughout the medium for analysis as the medium passes through the dosage form.

On the other hand, in **USP Apparatus 2**, paddle apparatus implies that there is a stationary vessel filled with a dissolution medium where a paddle will rotate at a specific speed. The bottom of the vessel holds this drug product while

hydrodynamic environment created by paddling is reproducible. It allows observation and testing of dissolution behavior under standardized conditions by regulation of paddle speed and temperature of medium.

### **Tell me the Name of the USP Chapter number for Dissolution.**

As per *USP Chapter No. 711* represents dissolution.

### **What is Q Value in Dissolution?**

The “Q” value is a percentage that shows how much of the dissolved active ingredient specified in the individual monograph there is.

### **What should be the temperature of the dissolution medium?**

The temperature of the dissolution medium should be  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ .

### **How does the Temperature affect the Dissolution Rate?**

Increase in temperature will increase the rate of drug dissolution which can result in effective breaks of tablets or capsules so temperature plays an important role.

### **What should be the pH of the Dissolution medium?**

pH medium should be in the range of  $5^{\circ}\text{C}$  to  $7^{\circ}\text{C}$  but can vary on condition.

### **Why does stirring increase the rate of dissolution?**

To distribute solute particles across the solvent, it must be stirred or agitated.

### **How to Increase the Dissolution Rate.**

**The dissolution rate can be increased for various reasons:**

- a) Decrease in particle size
- b) Increase in temperature
- c) Increase the stirring speed.

## **What is a Dissolution profile?**

Dissolution profile is an in vitro study to identify the %age of drug dissolved at different time intervals.

## **How to select Dissolution medium.**

It is based on the drug substance and formulation characteristics and interaction among compounds, and before starting analysis, we have to follow the respective product Standard Test Specification (STP) to know the dissolution medium.

## **Why Sinkers are used in Dissolution Test:**

Sinkers are used for floating tablets or capsules to set down. For capsules and sticky nature of tablets, sinkers are used.

## **What should be the water level in the Dissolution Water Batch?**

We should always check the recommendations of the manufacturer of the dissolution equipment. The water bath level should always be above that of dissolution medium in the vessel.

## **For Physical calibration of Dissolution test apparatus, what instruments are required?**

The instruments like Tachometer, stopwatch, Thermometer, Wobble Meter, Depth gauge, Digital Protractor, Vernier Caliper, and Centering Device are used.

## **For Physical calibration of Dissolution test apparatus, what parameters are to be checked/verified?**

The parameters are RPM Calibration, Calibration of Temperature Controller, Calibration of Timer, Wobble Check for Basket/Paddle, Distance from Bottom of Paddle/Basket to the bottom of the vessel, Jar Centering for basket and paddle,

Leveling of Instrument, Shaft Verticality of Basket/Paddle, and Sieve Integrity Check of the Basket.

## **Which Tablets are used in the calibration of Dissolution test apparatus?**

*Prednisone Tablets 10 or 50 mg* (Disintegrating Type) for Paddle methods and Salicylic acid for Basket methods are used for the calibration of dissolution test apparatus.

## **How do you Determine the Endpoint in Dissolution Testing?**

The endpoint for dissolution tests is usually considered to be reached when a predetermined amount of the active substance has dissolved in a given time period. Therefore, UV spectrophotometry, high-performance liquid chromatography (HPLC), or any other suitable chemical and physical methods can be used to evaluate such a point. Usually, monographs on drugs, as well as regulatory guidance documents, give specifications for endpoints based on parameters such as percentage of drug dissolved. Also, some extended-release formulations may have several endpoints at various time intervals within the duration of release.

## **What is the importance of validation in Dissolution testing?**

Validation is an essential aspect of dissolution testing which ensures that the test method used is reliable, reproducible, and appropriate for its intended purpose. This process plays a critical role in determining the accuracy and reliability of findings needed for regulatory approval and quality control. Different parameters like specificity, linearity, accuracy, precision, range, and robustness are checked during the validation process. This means that validated methods will enable batch-to-batch consistency comparison between products as well as assess drug product stability confirming formulation equivalence. It also ensures that any changes in the manufacturing process or the scale-up of production do not negatively impact the product's quality.

## **What is Aliquot withdrawal position in Dissolution?**



Samples are taken from midway between the top of the paddle/basket and the surface of the dissolving medium, about *at least 1cm* away from the container wall.

### **What concentrations of Hydrochloric acid are appropriate for use as Dissolution media?**

A range of Hydrochloric acid from *0.1 N* to about *0.001 N* is recommended to be used as a dissolution medium.

### **What pore-size filters should be used in Dissolution testing?**

The filter pore size can range from *0.45  $\mu\text{m}$*  to *70  $\mu\text{m}$* . However, if the filtrate has a cloudy appearance, or the filter becomes clogged, an alternative type of filter or pore size should be evaluated.

### **What are the Mesh sizes of baskets that can be used in Dissolution?**

USP General **Chapter <701> Dissolution**. The sizes are *40 (default), 20, and 10 mesh*. Any other mesh size can be used with appropriate justification.

### **What are Acceptance Criteria for Dissolution as per USP?**

The dissolution acceptance criteria set out in the United States Pharmacopeia (USP) depend on the nature of both the drug being examined and its dosage form. The content of a standard can be compared to dissolution profiles for such information.

#### **Immediate Release Solid Oral Dosage Forms:**

The drug must dissolve not less than *85%* as indicated by their label within *30 minutes*.

#### **Extended-Release Solid Oral Dosage Forms:**

Different dissolution conditions are applied according to the type and release mechanism of a drug. In general, most formulations need to have between 80% and 90% dissolved within a specified period.

### **Topical Dosage Forms:**

A minimum of seventy percent of the active ingredient should be released within specific time limits.

### **Oral Suspensions:**

Dissolution rate: at least 30% must dissolve within first hour

### **Inhalation Products:**

At least eighty percent should be dissolved within a specified period.

### **Do air bubbles affect the Dissolution of the drug?**

Yes, it affects. Tablets may retain air bubbles leading to alteration of the drug dissolution rate.

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