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REVIEW ON DISSOLUTION APPARATUS

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ABSTRACT

In this review paper we will focus on different dissolution process and different types of dissolution apparatuses are in use. Dissolution research started to develop about 100 years ago as a field of physical chemistry . Dissolution test is required to study the drug release from the dosage form and its in vivo performance.in this review paper we done the tablet dissolution of metoprolol succinate and measured that time of release. Dissolution test is used to assess the lot to lot quality of drug product. The development and validation of dissolution procedures is of paramount importance during development of new formulation and in quality control.[7] Dissolution Apparatus performed quality control tests for the oral solid dosage forms

KEYWORDS:- *Dissolution Testing, USP Apparatus, USP Apparatus 1 (Basket Method) USP Apparatus 2 (Paddle Method), In-vitro Dissolution, Tablet Dissolution, Drug Release Rate Profiling*

1.INTRODUCTION

- Dissolution is the process where a solid medicine breaks down in a specific amount of liquid. How well a medicine dissolves affects how well the body absorbs it. [1]
- the study of the dissolution process has been developing since the end of the 19th century by physical chemist
- The first studies on dissolution were reported in 1897 *by Noyes and whitney* in the litera ture
- The dissolution apparatus is a fundamental tool in pharmaceutical research and development, primarily used to evaluate the release of active pharmaceutical ingredients (APIs) from solid dosage forms, such as tablets and capsules. This evaluation is crucial for ensuring the efficacy and safety of medications.

➢ 1.1 Types of Apparatus (IP):

- **Apparatus 1 (Basket)**: This apparatus uses a basket that holds the dosage form and allows it to be submerged in the dissolution medium. It is particularly useful for formulations that are prone to floating or settling.[2]
- **Apparatus 2 (Paddle)**: In this configuration, a paddle stirs the dissolution medium, and it is commonly used for a wide variety of solid dosage forms.[2]

➢ 1.2 Dissolution apparatus plays important role in:

- **Drug Development**: The dissolution apparatus plays a vital role in the formulation development stage, helping researchers optimize the release profile of drugs to achieve desired therapeutic effects.[4]
- **Quality Control (QC)**: It is a standard test in QC processes to ensure that the final product meets specific dissolution criteria, providing assurance of batch consistency.[4]
- **Biopharmaceutical Studies**: The results from dissolution testing can help predict the in vivo performance of drugs, influencing decisions about bioavailability and therapeutic effectiveness.[4]

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1.3 Types of Dissolution Appratus

Table:1[6][7]

	I.P	U.S.P	B.P	E.P
TYPE 1	Paddle Apparatus	Basket Apparatus	Basket Apparatus	Paddle Apparatus
TYPE 2	Basket Apparatus	Paddle Apparatus	Paddle Apparatus	Basket Apparatus
TYPE 3		Reciprocating Apparatus	Flow through Cell Apparatus	Flow through Cell Apparatus
TYPE 4		Flow through Cell Apparatus		
TYPE 5		Paddle over disc Apparatus		
TYPE 6		Rotating cylinder		
TYPE 7		Reciprocating Holder		

2. MAJOR CONTRIBUTIONS AND EVENTS IN THE DEVELOPMENT OF DISSOLUTION TESTING

Table 2 [1]

Year	Contributor (s)	Major contribution
1897	Noyes AN and Whitney WR	Conducted the first dissolution experiments and published an article entitled “the rate of solution of solid substances in their own solutions”. Noyes- Whitney equation
1900	Brunner E and von Tolloczko S	Showed that the rate of dissolution depends on the exposed surface, the rate of stirring, temperature, structure of the surface and the arrangement of the apparatus
1904	Nernst W and Brunner E	Nernst–Brunner equation based on the diffusion layer concept and Fick's second law.
1931	Hixson AW and Crowell JH	Dependence of reaction velocity upon surface and agitation. Hixson and Crowell reported that the Noyes–Whitney equation in its original form and without any details about the mechanism of the process had been sufficiently validated with a wide range of experiments, as opposed to the various mechanistic explanations that had appeared, none of which was entirely satisfactory.
1951	Edwards Lj	First to appreciate that following the oral administration of solid dosage forms, if the absorption process of drug from the gastrointestinal tract is rapid, then the rate of dissolution of that drug can be the step which controls its appearance in the body
1957	Nelson E	First to explicitly relate the blood levels of orally administered drugs (theophylline salts) to their in vitro dissolution rates.
1961	Higuchi T	Reviewed the interfacial barrier model proposed by Wilderman in 1909 and Danckwerts model (1951)
1962	Levich VG	Improved the theoretical model of the dissolution experiment using rotating disks, taking into account the centrifugal force on diffusion.

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1970		The basket-stirred-flask test (USP apparatus 1) was adopted as an official dissolution test in 6 monographs of the United States Pharmacopeia (USP) and National Formulary (NF)
1978		Adoption of the paddle method (USP apparatus 2)
1981		The first guidelines for dissolution testing of solid dosage forms were published as a joint report of the Section for Official Laboratories and Medicines Control Services and the Section of the industrial pharmacist FIR
1991		Adoption of the reciprocating cylinder (USP apparatus 3) for extended-release products..
1995		Adoption of the flow-through cell in (USP apparatus 4) for extended-release products.

3.TYPES OF DISSOLUTION APPARATUS(IP)

3.1. Basket Dissolution Apparatus

The basket dissolution apparatus is a widely used instrument in pharmaceutical laboratories for evaluating the dissolution characteristics of solid oral dosage forms, such as tablets and capsules. This apparatus helps determine how quickly and efficiently a drug dissolves in a liquid medium, which is critical for assessing its bioavailability and overall performance.[10]

Basket Dissolution Apparatus

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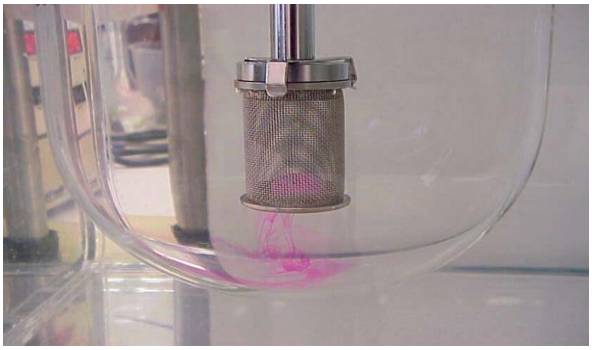


Basket that Hold The Dosage form (tablet, capsul)

- **Key Components**: [11]

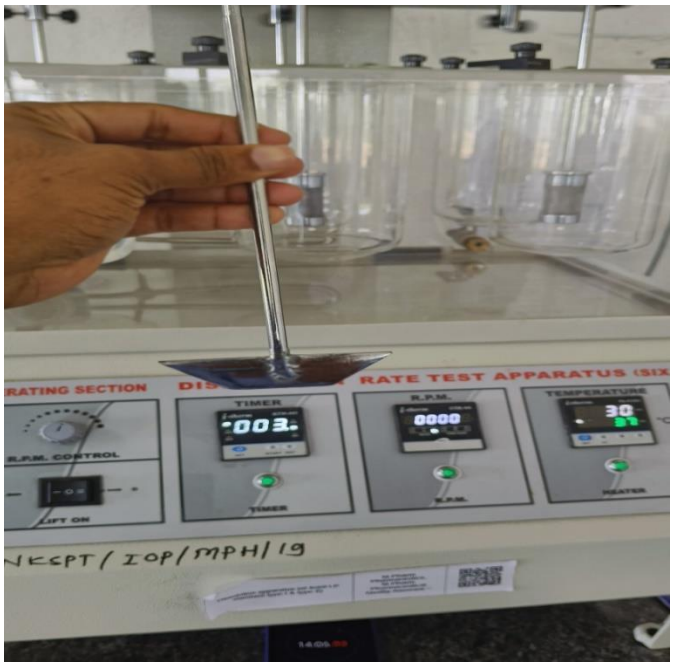
1. **Basket**: A mesh or perforated container that holds the dosage form during the dissolution test.
2. **Motorized Drive**: Mechanism to lower and raise the basket into and out of the dissolution medium
3. **Dissolution Medium**: A specific volume of solvent (often water or simulated gastric fluid) that mimics physiological conditions.
4. **Temperature Control**: Heating system to maintain the medium at a constant temperature, usually around 37°C.
5. **Sampling System**: Allows for the collection of samples from the dissolution medium at predetermined intervals.

- **Objectives**

1.**Measuring Dissolution Rate**: To find out how fast a drug releases its active ingredients.[5]
2.**Comparing Formulations**: To check differences between various drug formulations or batches.[9]
3.**Quality Control**: To ensure products meet required dissolution standards for safety and effectiveness.
4.**Predicting Drug Absorption**: To help estimate how well the drug will work in the body.[12]

3.2. Paddle Dissolution Apparatus

The paddle dissolution apparatus is a device used to measure the dissolution rates of solid oral dosage forms, such as tablets and capsules. It operates on similar principles as the basket dissolution apparatus but uses a paddle to stir the dissolution medium



Paddle Dissolution Apparatus

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- **Purpose and Application**
  - **Dissolution Testing**: The primary purpose of the paddle dissolution apparatus is to test how a drug dissolves in a specific medium. The results help ensure the drug will dissolve at an appropriate rate in the gastrointestinal tract after ingestion.
  - **Quality Control**: It is used to confirm the consistency and reliability of drug formulations, ensuring batch-to-batch uniformity in the dissolution characteristics of the product.
  - **Regulatory Requirements**: Dissolution testing is a crucial part of the drug approval process, and dissolution data is often required by regulatory agencies (e.g., FDA, EMA) to ensure that a drug releases its active ingredient at a predictable and effective rate.

- **Key Components**: [8][5][12]

1.Dissolution Vessel: A container that holds the dissolution medium (usually a liquid) where the drug is tested.
2.Paddle: A rotating paddle that stirs the medium, ensuring even distribution and mimicking gastrointestinal conditions.
3.Heating Element: A system to maintain the temperature of the dissolution medium, as temperature can affect drug solubility.
4.Drive Mechanism: A motor that controls the rotation speed of the paddle, which can be adjusted according to testing requirements.
5.Sampling Port: An area where samples of the dissolution medium can be taken at specified intervals to analyse the concentration of the dissolved drug.
6.Data Collection System: Equipment or software that records the dissolution data, which is essential for analysis and reporting.

- **Objectives**: [12] [5]

1. **Dissolution Rate Measurement**: To determine how quickly a drug dissolves in a fluid, simulating conditions in the gastrointestinal tract.
2. **Comparative Testing**: To compare the dissolution profiles of different formulations or batches to ensure consistency and effectiveness.
3. **Quality Control**: To verify that pharmaceutical products meet regulatory standards for dissolution, which is crucial for their efficacy.
4. **Predicting Bioavailability**: To estimate how well and quickly a drug will be absorbed in the body based on its dissolution characteristics.

4. METOPROLOL SUCCINATE DISSOLUTION TIME AND PERCENTAGE DISSOLVE OF DRUGS IN (IP1 & IP2) APPARATUS

- **4.1 Metoprolol succinate**

Metoprolol succinate is a medication that belongs to a class of drugs known as beta-blockers. It is commonly used to treat high blood pressure, heart failure, and to prevent angina (chest pain). It works by blocking beta-adrenergic receptors in the heart, leading to a decrease in heart rate and blood pressure, which helps reduce the heart's workload.

The dissolution time of **metoprolol succinate ER tablets** is designed to ensure a **gradual release over 24 hours**. In in vitro testing, the full release of the drug may occur over **8 to 24 hours**, depending on the formulation and testing conditions.[22]

- **Used for**
- **Hypertension (High Blood Pressure):** It helps lower blood pressure, reducing the risk of stroke and heart attack.[13]

- **Heart Failure:** It is used as part of the treatment regimen for chronic heart failure, helping to improve symptoms and reduce hospitalizations.[6]

- **Angina Pectoris:** Metoprolol succinate can relieve chest pain associated with angina.[14]

- **Post-Myocardial Infarction:** It is often prescribed after a heart attack to improve survival and reduce the risk of further heart issues.[15]

- **Arrhythmias:** It may be used to manage certain types of irregular heartbeats.[16]

- **Migraine Prophylaxis:** Occasionally, it is used to prevent migraines.[17]

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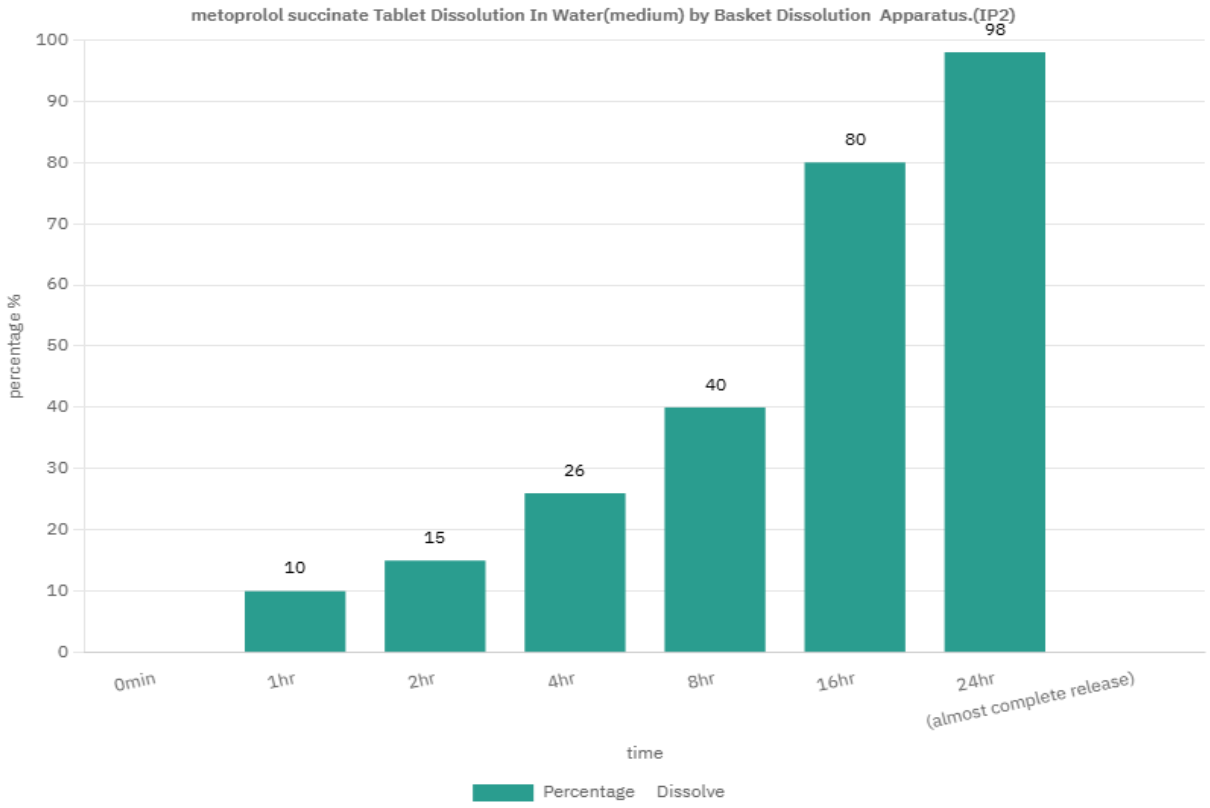
➢ **4.2. Tablet Dissolution In Water(medium) by Basket Dissolution Apparatus.(IP2)**

Time (hour)	Percentage Dissolve
0min	0%
1hr	10%
2hr	15%
4hr	26%
8hr	40%
16hr	80%
24hr	98% (almost complete release)



➢ **4.3. Tablet Dissolution In Water(medium) by Paddle Dissolution Apparatus(IP1)**

Time (hour)	Percentage Dissolve (%)
0min	0%
1hr	12%
2hr	24%
4hr	30%
8hr	50%
16hr	77%
23hr	99% (Dissolve)

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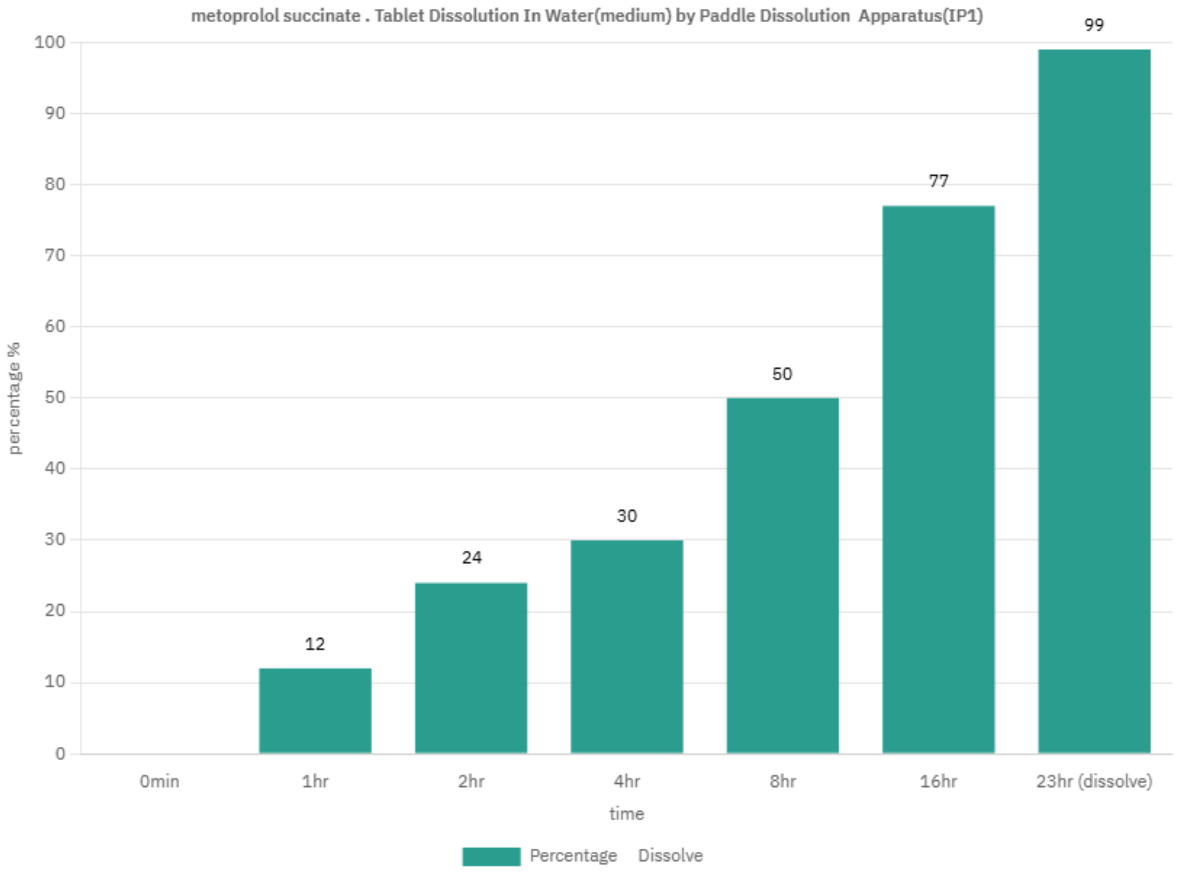

➢ **4.4. Tablet Dissolution In Alcohol(medium) by Basket Dissolution Apparatus.(IP2)**

Time (min)	Percentage Dissolve
0min	0
10min	11.47%
20min	18.03%
30min	25.81%
40min	32.37%
50min	39.75%
1hr	47.13%
1hr 20min	55.73%
1hr 40min	73.77%
1hr 50min	Dissolve

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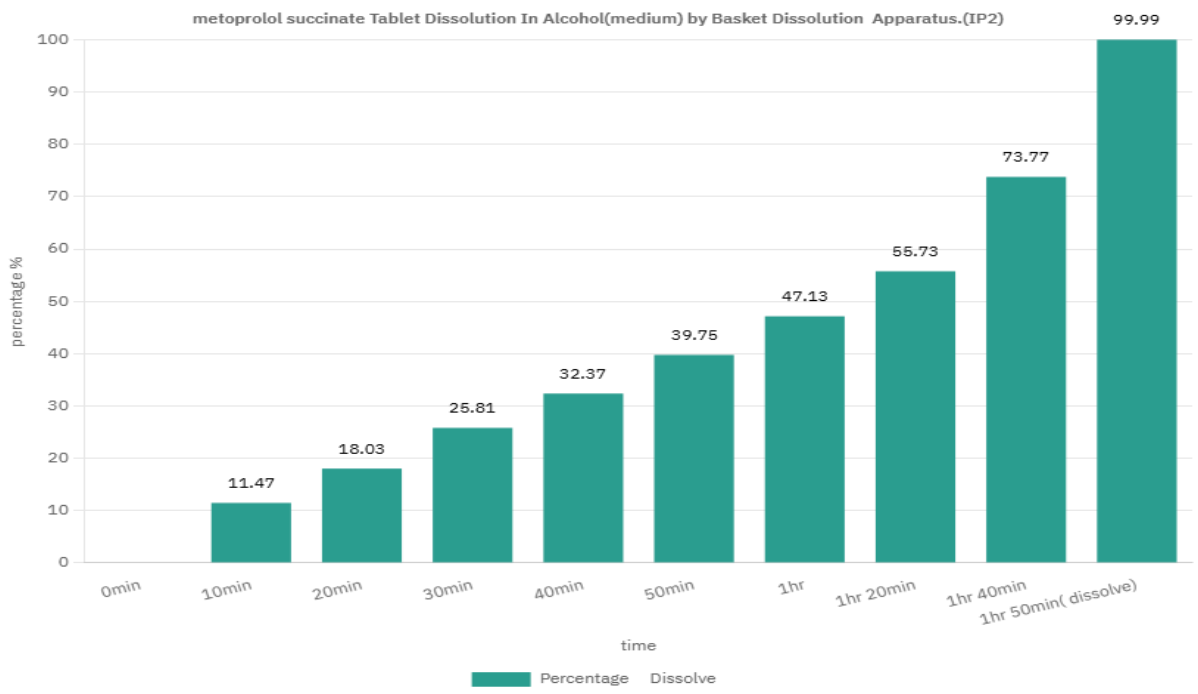

- **Dissolution Time in Alcohol**: [20][21]
  metoprolol succinate These tablets are made to release the drug slowly over many hours. But when tested in alcohol, they might **dissolve much faster**, potentially in **30 minutes to 2 hours**.
  Why? Alcohol can disrupt the slow-release mechanism (like the coating or the matrix inside), causing the drug to be released **too quickly**.

➢ **4.5. dissolution testing involves several key steps** [8][9]

1.Selection of Drug Formulation

- Choose the specific drug formulation (e.g., tablets, capsules) you want to test.

2. Preparation of Dissolution Medium

- **Choose Medium**: Select an appropriate dissolution medium based on the drug's solubility characteristics. Common media include:
  - Water
  - 0.1 N Hydrochloric Acid
  - Phosphate Buffer (pH 4.5 or 6.8)
  - Alcohol(Lab Solvent)
- **Temperature Control**: The medium is typically maintained at 37 °C to mimic physiological conditions.

3. Apparatus Setup

- **Select Dissolution Apparatus**: Common options include:
  - **USP Apparatus 1 (Basket Method)**
  - **USP Apparatus 2 (Paddle Method)**
- Ensure the apparatus is calibrated and functioning correctly.

4. Weighing and Placing the Drug

- **Accurate Weighing**: Weigh the drug dosage form (e.g., tablet) accurately.
- **Placement**: Place the dosage form in the dissolution vessel.

5. Initiating the Dissolution Test

- **Start the Apparatus**: Turn on the apparatus to begin the dissolution process.
- **Set Time Intervals**: Determine the time points for sampling (e.g., 5, 10, 15, 30 minutes).

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6. Sampling

- At each time interval, withdraw a specified volume of the dissolution medium.
- Measure the weight of the drug .

7. Data Analysis

- **Calculate Percentage Dissolved**: Use the concentration data to calculate the percentage of the drug that has dissolved at each time point.
- **Plot Dissolution Profile**: Create a graph of percentage dissolved versus time for analysis.

8. Quality Control

- **Repeat Testing**: Conduct the test in duplicate or triplicate to ensure reliability.
- **Compare to Standards**: Check the results against pharmacopoeial standards to ensure the formulation meets specifications.

5. CONCLUSION

Dissolution apparatus are important tools used in the pharmaceutical industry to test how a drug releases its active ingredients when it dissolves in the body. This helps scientists understand how quickly and completely a drug will be absorbed after it is taken. The most commonly used types of dissolution apparatus are **Apparatus 1 (Basket Method)** and **Apparatus 2 (Paddle Method)**, each designed for different types of drug formulations like tablets and capsules. [19]

It's essential to make sure that the dissolution apparatus are set up correctly and consistently, with factors like temperature, agitation speed, and the type of liquid (dissolution medium) being controlled. This ensures that the results are accurate and repeatable. The **FDA (U.S. Food and Drug Administration)** and the **European Medicines Agency (EMA)** provide strict guidelines to ensure that these tests are done properly. [18]

6.RESULT

1.Metoprolol succinate tablet Dissolves faster In alcohol compared to water and any other medium.
2.When **metoprolol succinate extended-release tablets** are dissolved in alcohol, the release of the drug can **happen faster** than intended. This is because alcohol can affect the way the tablet dissolves, making it break down more quickly.

NOTE

As a result, drinking alcohol with this medication can lead to higher levels of the drug in your bloodstream, which may increase the risk of side effects or even overdose.
To be safe, it is generally recommended to avoid drinking large amounts of alcohol while taking metoprolol succinate extended-release.

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