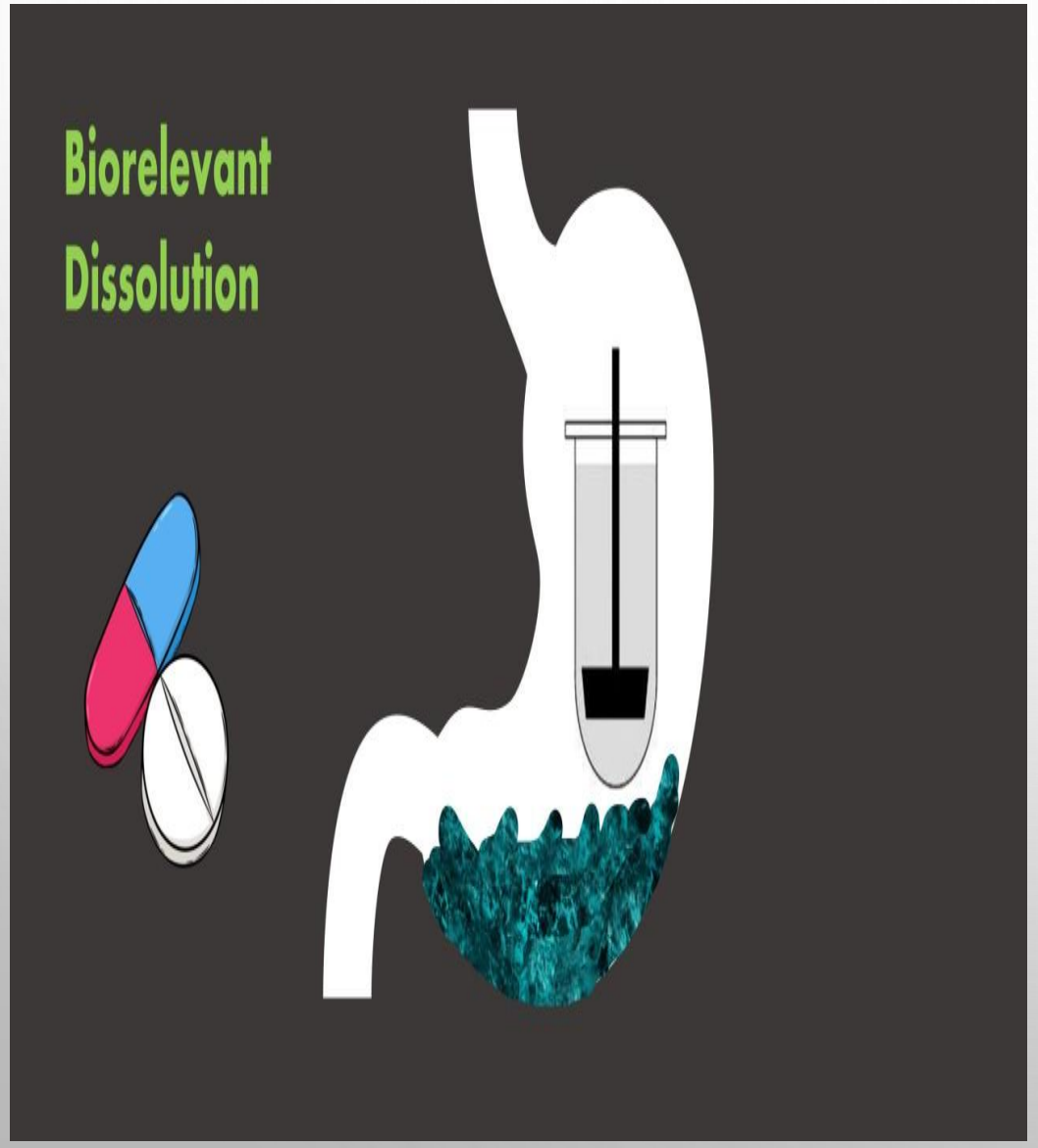
IN VITRO DISSOLUTION STUDY OF PER – ORAL TABLET



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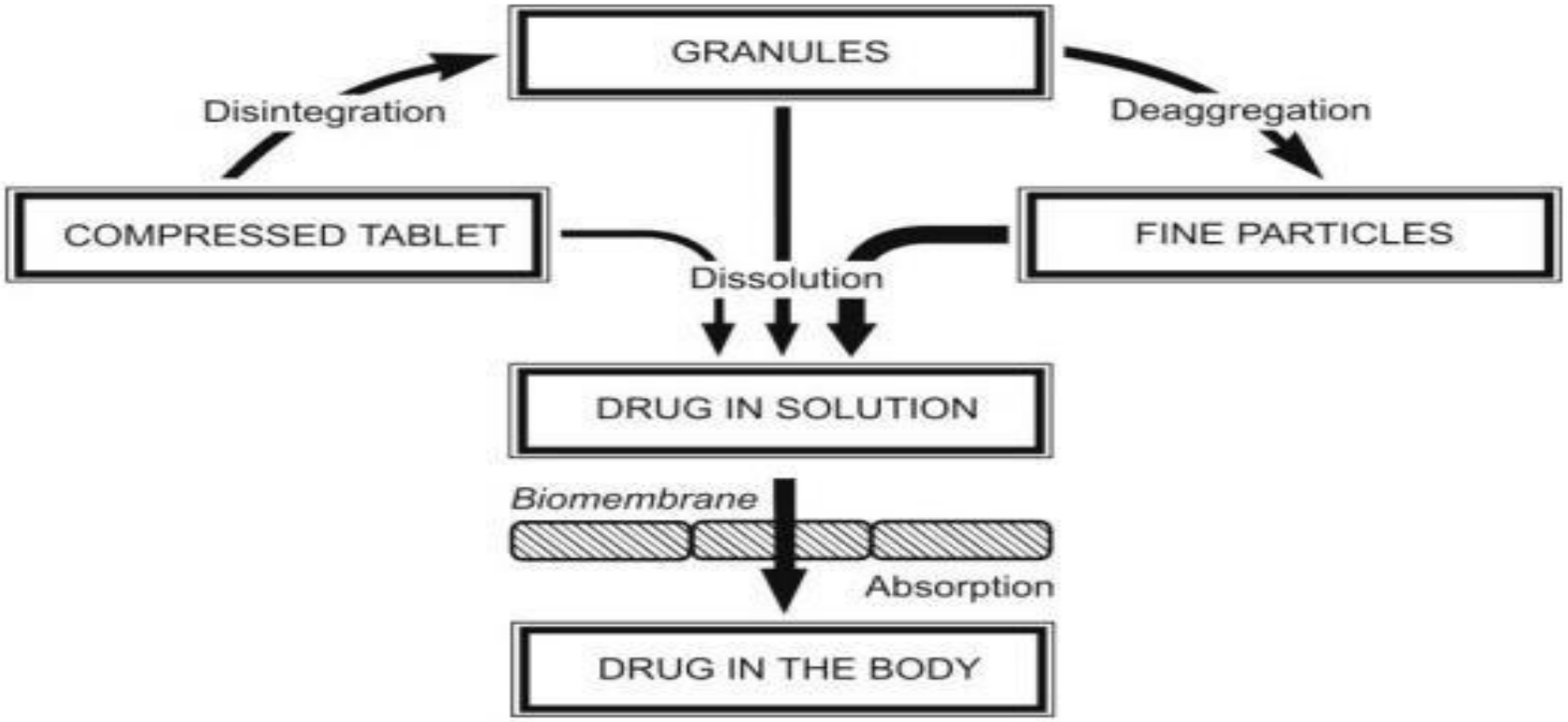
INTRODUCTION :

- **DISSOLUTION IS A PROCESS OF GOING INTO SOLUTION FORM .**
- **A BASIC PRINCIPLE OF DRUG ABSORPTION IS THAT ABSORPTION TAKES PLACE ONLY AFTER A DRUG IS IN SOLUTION.**
- **THIS MEANS THAT DRUG GIVEN ORALLY IN SOLID DOSAGE FORM MUST DISSOLVE IN GIT FLUID BEFORE ABSORPTION OCCURS**

The following process occurs before absorption of solid dosage forms

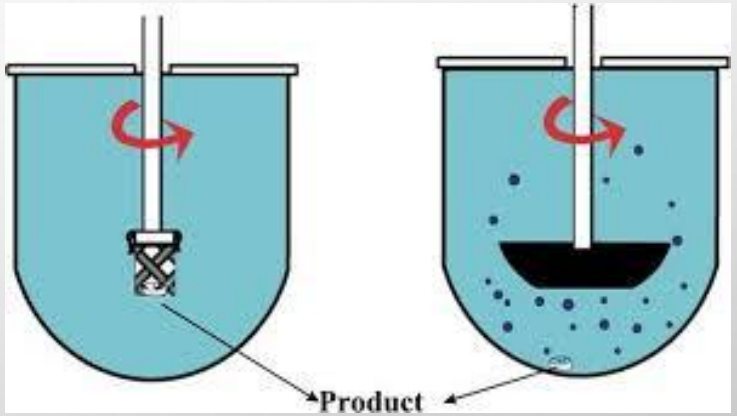


- **DISSOLUTION RATE** : IS DEFINED AS THE AMOUNT OF SOLID SUBTANCE THAT GOES INTO SOLUTION PER UNIT TIME UNDER STANDARD CONDITION OF TEMPERATURE, PH AND SOLVENT COMPOSITION

- DISSOLUTION IS THE **RATE LIMITING STEP** FOR HYDROPHOBIC POORLY SOLUBLE DRUG FOR EXAMPLE, GRISEOFULVIN AND SPIRONOLACTONE

Factors affecting dissolution rate

- Agitation intensity
- Drug solubility
- Surface area exposed to dissolution medium



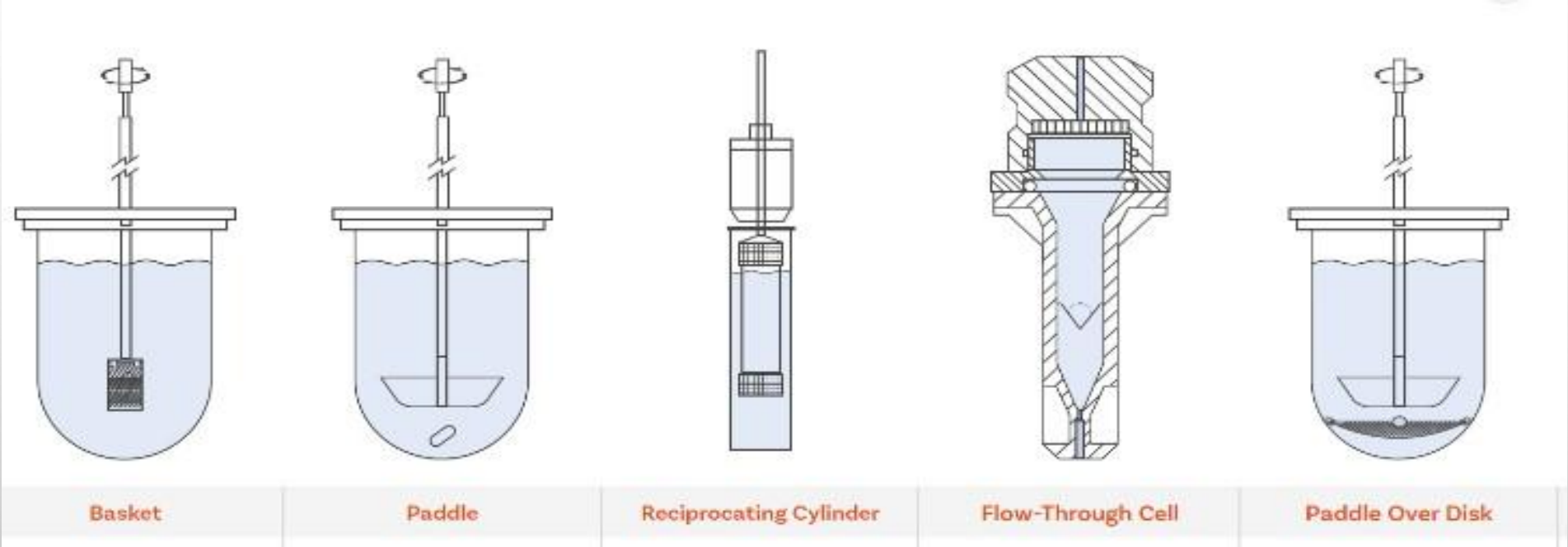
EXPRESSION OF SOLUBILITY

Descriptive term	Parts of solvent required for 1 part of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10,000
Practically insoluble or insoluble	More than 10,000

BCS CLASSIFICATION

BCS Class	Solubility	Permeability	Examples of Drugs	Formulation / Bioavailability Considerations
Class I	High	High	Metoprolol, Propranolol, Verapamil, Acetaminophen	Usually good oral absorption; dissolution is rate-limiting. Standard immediate-release (IR) formulations are suitable.
Class II	Low	High	Ketoconazole, Danazol, Carbamazepine, Ibuprofen	Dissolution is the limiting step. Use solubility enhancement techniques (e.g., nanoparticles, solid dispersions, surfactants).
Class III	High	Low	Metformin, Cimetidine, Atenolol, Ranitidine	Permeability is rate-limiting. Formulation focuses on permeability enhancers or transporter considerations.
Class IV	Low	Low	Hydrochlorothiazide, Furosemide, Paclitaxel	Poor oral bioavailability; requires special delivery systems (nanofibers, nanoparticles, lipid carriers).

TYPES OF DISSOLUTION APPARTUS (USP)



I. Capsules, floating forms	II. Tablets (IR & ER)	III. Controlled-release, pH changes	IV. Poorly soluble drugs, implants	V. Transdermal patches

WHAT IS SINK CONDITION?

Imagine a **sink with running water.**

- When you dissolve sugar in a **big sink with flowing water,** the sugar **keeps dissolving easily** because the water is always fresh.
- The sugar never accumulates = **sink condition.**

But if you dissolve sugar in a **small cup,** it becomes full quickly and no more sugar dissolves = **non-sink condition.**

- DISSOLUTION TESTS CAN BE CONDUCTED IN SIMPLE BUFFER SOLUTIONS OR IN MORE BIO-RELEVANT DISSOLUTION MEDIA.

- DISSOLUTION TESTS ARE NORMALLY PERFORMED **UNDER SINK CONDITIONS** (THE DISSOLUTION MEDIUM SHOULD NOT BECOME "FULL" OF DRUG; IT SHOULD STILL BE ABLE TO DISSOLVE MORE).

- **SINK CONDITION** IS THE ABILITY OF THE DISSOLUTION MEDIA TO DISSOLVE AT LEAST 3 TIMES THE AMOUNT OF DRUG THAT IS IN YOUR DOSAGE FORM.

Rule of thumb

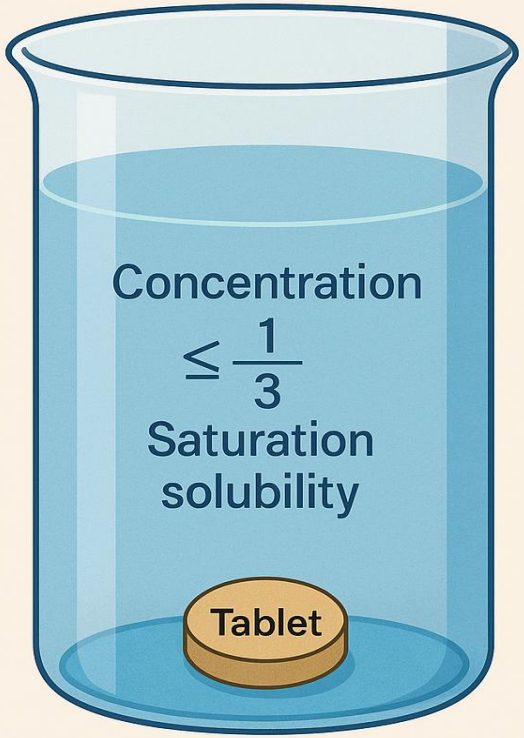
Sink condition is considered adequate when:

$$V \geq 3 \times \frac{\text{Dose}}{\text{Solubility } (\frac{mg}{ml})}$$

- HAVING SINK CONDITIONS HELPS YOUR DISSOLUTION HAVE MORE ROBUSTNESS AS WELL AS BEING MORE BIOLOGICALLY RELEVANT.

SINK CONDITION

Sink condition exists when the **volume of dissolution medium is large enough** that the **drug concentration never exceeds 10–30% of its saturation solubility.**



Large volume

If Sat. Solubility of drug = (5mg/ml) then if use 900 ml = 4500 mg

Then if we add 50 mg * 3 = 150 mg

WHY IS SINK CONDITION IMPORTANT?

BECAUSE IF THE MEDIUM BECOMES SATURATED:

1. DISSOLUTION RATE SLOWS DOWN OR STOPS
2. PRECIPITATION MAY OCCUR
3. RESULTS BECOME INACCURATE
4. YOU CANNOT COMPARE FORMULATIONS PROPERLY
5. IT NO LONGER FOLLOWS FIRST-ORDER DISSOLUTION KINETICS.

Example

Drug solubility = 1 mg/mL

Dose = 100 mg

Minimum medium for sink condition:

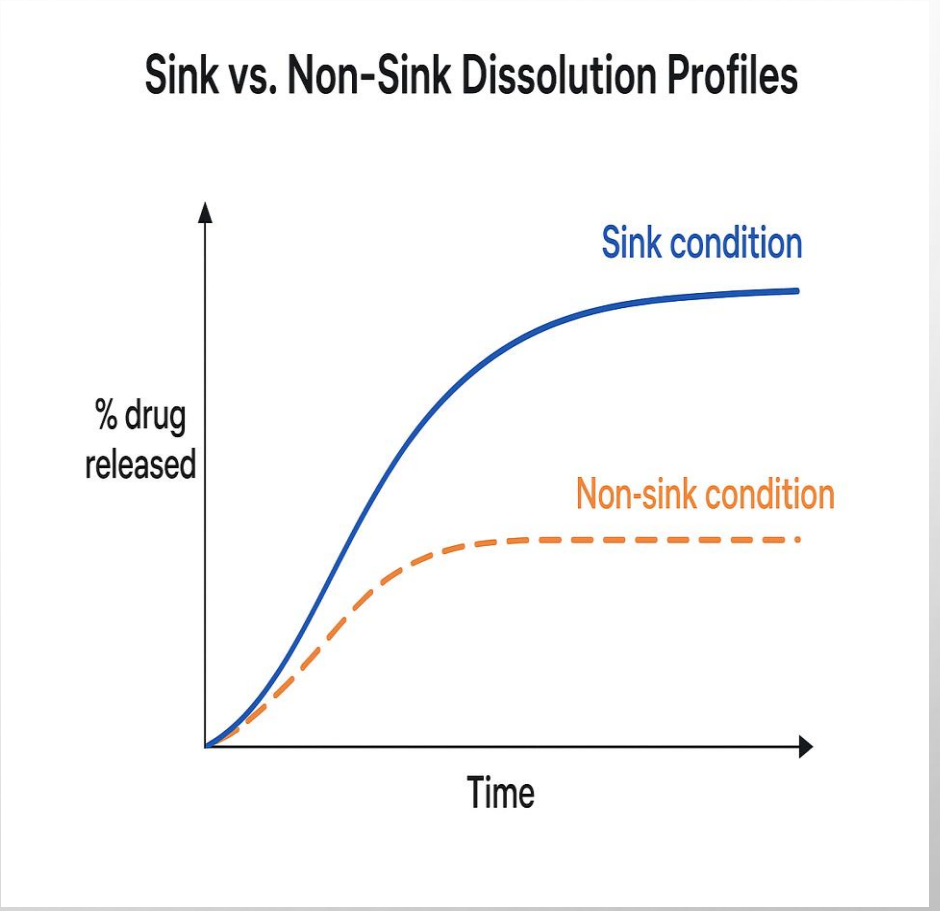
$$V = 3 \times \frac{100}{1} = 300\ mL$$

So, using **300 mL or more** ensures sink condition.

HOW TO MAINTAIN SINK CONDITION

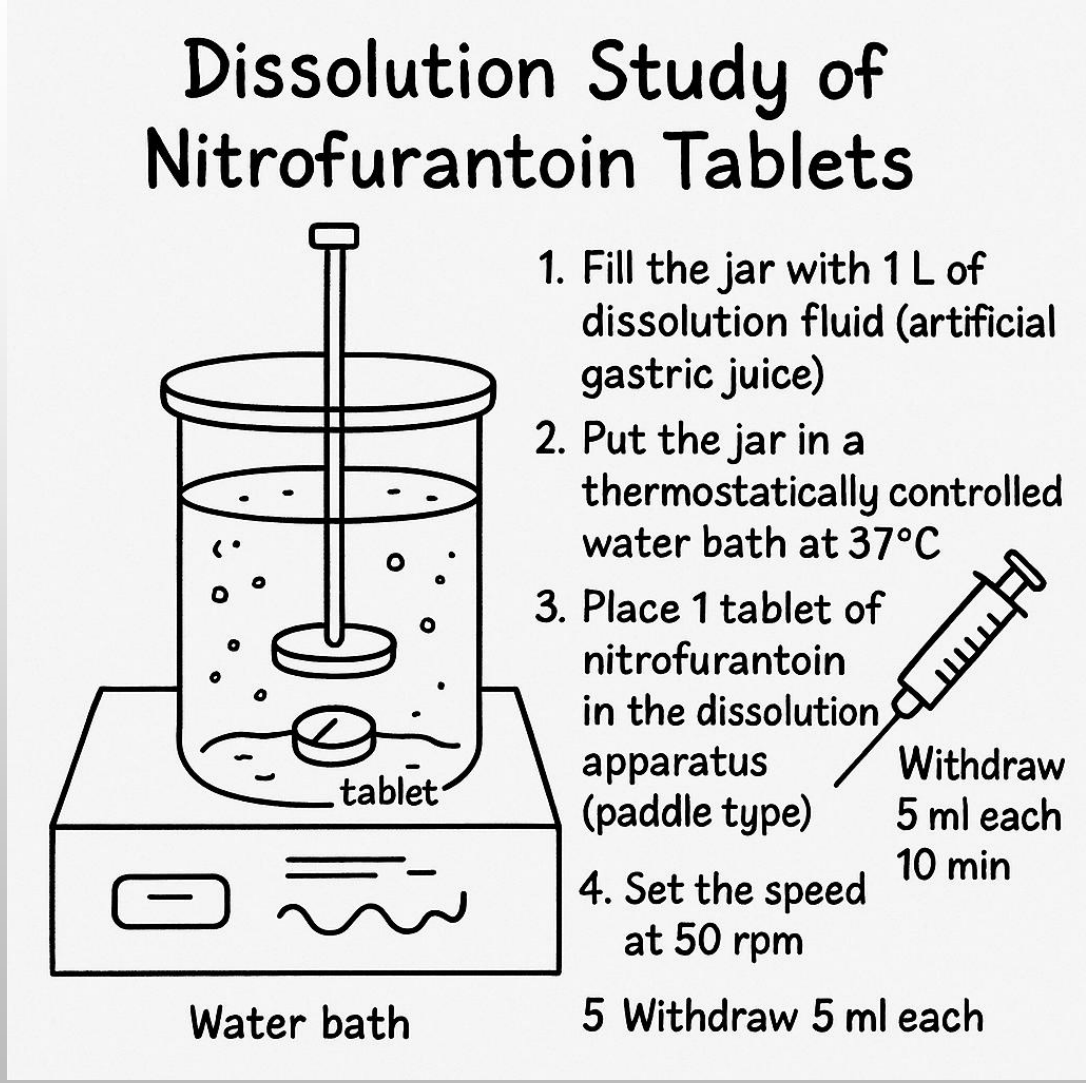
BECAUSE SOME DRUGS DISSOLVE VERY SLOWLY (POORLY SOLUBLE), WE CREATE SINK CONDITION BY:

1. **INCREASING MEDIUM VOLUME**
   (E.G., FROM 500 ML → 900 ML)
2. **ADDING SURFACTANTS**
   (SLS, TWEEN, ETC.)
3. **CHANGING PH**
   TO INCREASE IONIZATION → BETTER SOLUBILITY
4. **USING CO-SOLVENTS**
   (ETHANOL, PEG 400)
5. **INCREASING STIRRING SPEED**
   (50 → 75 RPM)



Procedure (Dissolution study of nitrofurantoin tablets)

- Fill the jars with 1 L of dissolution fluid (artificial gastric juice)
- Put the jars in a thermostatically controlled water bath at 37 °C (switch water bath on)
- Place 1 tablet of nitrofurantoin in the dissolution apparatus (paddle type).
- Set the speed on 50 r.p.m
- Withdraw 5 ml each 10 min for 50 minutes

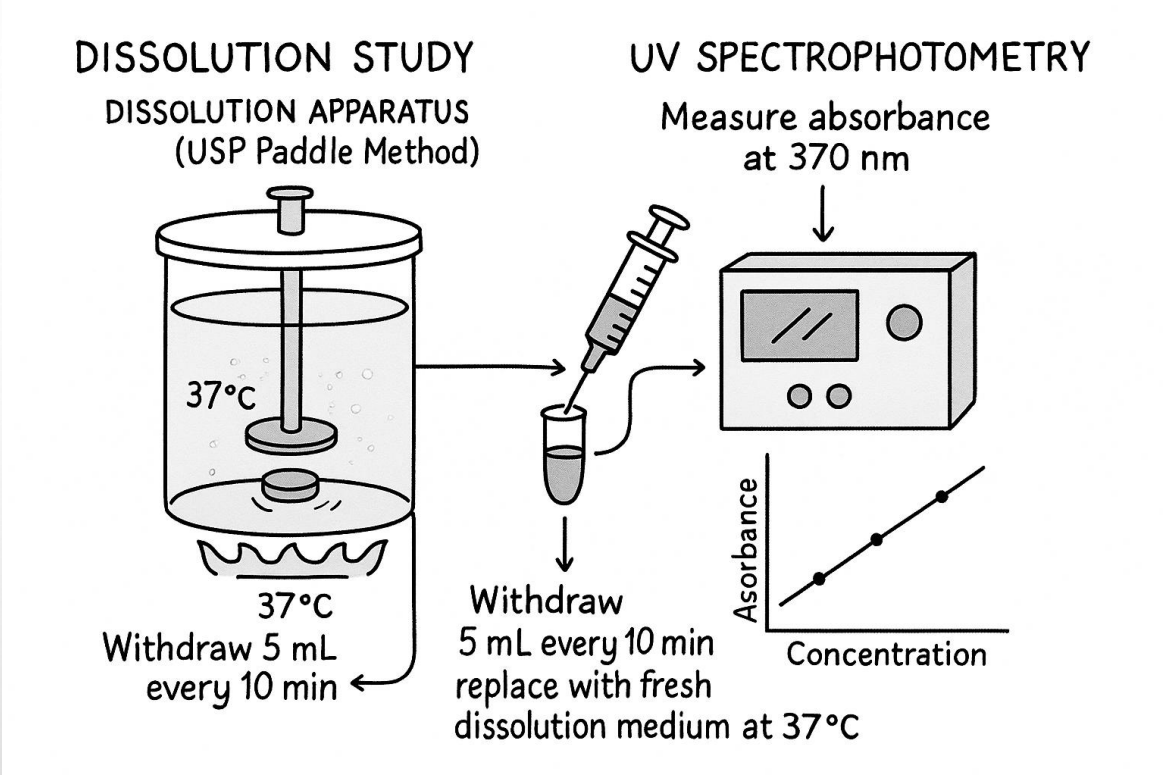


- Substitute for the volume withdrawn each time interval using a fresh (artificial gastric juice) previously maintained at 37º C

- Analyze samples of nitrofurantoin by reading the absorbance on a UV spectrophotometric

  at 370 nm.

- Use the straight line equation $y=0.0036+0.07x$ to obtain the concentration of the dilutions.
- Note : the conc. Is in mcg/ml

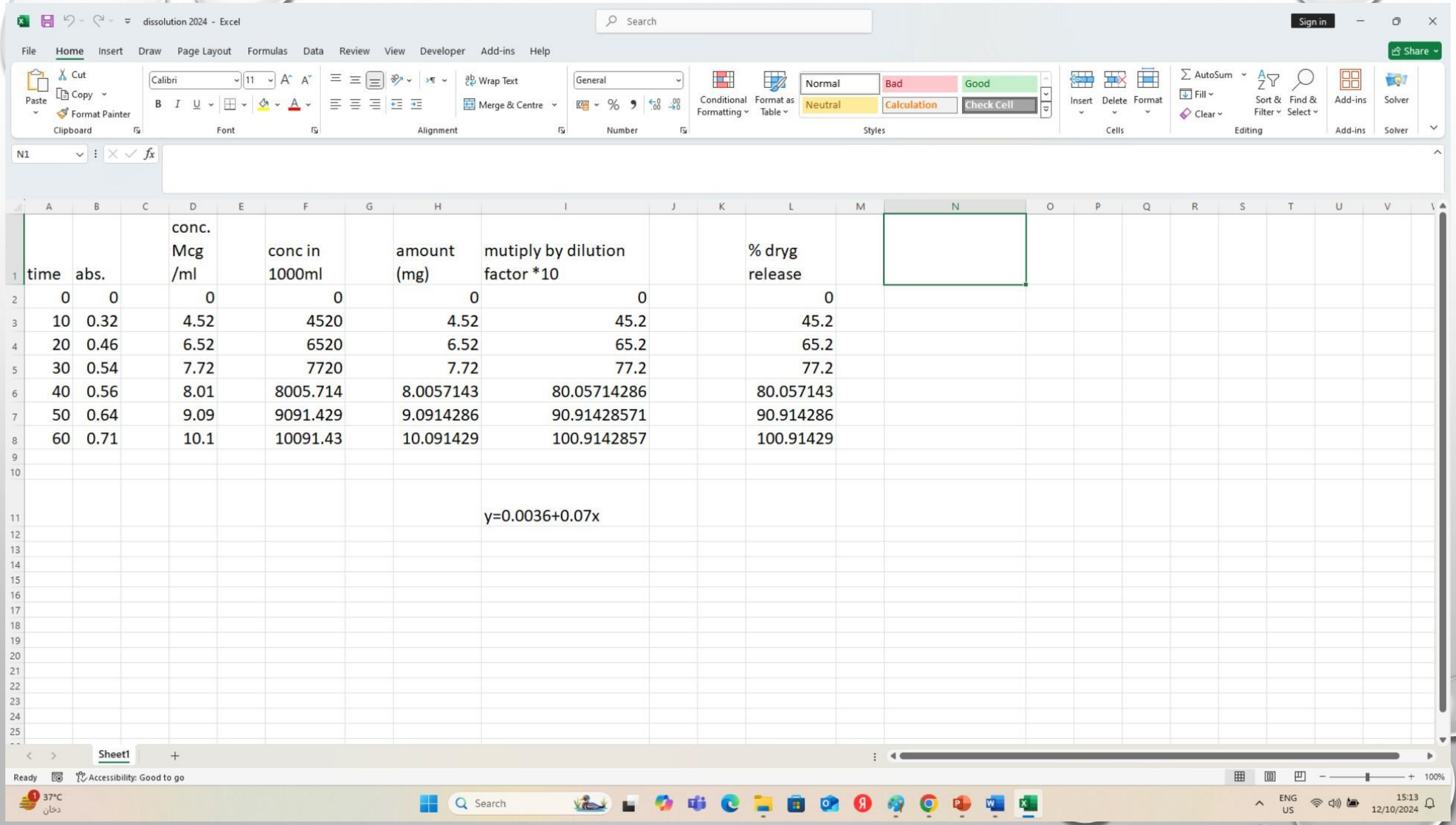


- 1-CON.(MCG/ML)X VOL. OF DISSOLUTION MEDIA =(MCG AMOUNT OF DRUG RELEASED INTO THE DISSOLUTION MEDIA THEN CONVERT IT TO MG

- 2- MULTIPLY THE AMOUNT WITH DILUTION FACTOR (IF YOU MADE DILUTION)

- 3-% OF DRUG RELEASED = AMOUNT OF DRUG RELEASE /AMOUNT OF DRUG IN THE TABLET *100

- 4- THEN PUT THE TIME COLUMN AND PERCENT OF DRUG RELEASE COLUMN TOGETHER THEN CLICK INSERT, SCATTER WITH SMOOTH LINES AND MARKERS



dissolution 2024 - Excel

time	abs.	conc. Mcg /ml	conc in 1000ml	amount (mg)	mutiply by dilution factor *10	% dryg release
0	0	0	0	0	0	0
10	0.32	4.52	4520	4.52	45.2	45.2
20	0.46	6.52	6520	6.52	65.2	65.2
30	0.54	7.72	7720	7.72	77.2	77.2
40	0.56	8.01	8005.714	8.0057143	80.05714286	80.057143
50	0.64	9.09	9091.429	9.0914286	90.91428571	90.914286
60	0.71	10.1	10091.43	10.091429	100.9142857	100.91429

y=0.0036+0.07x

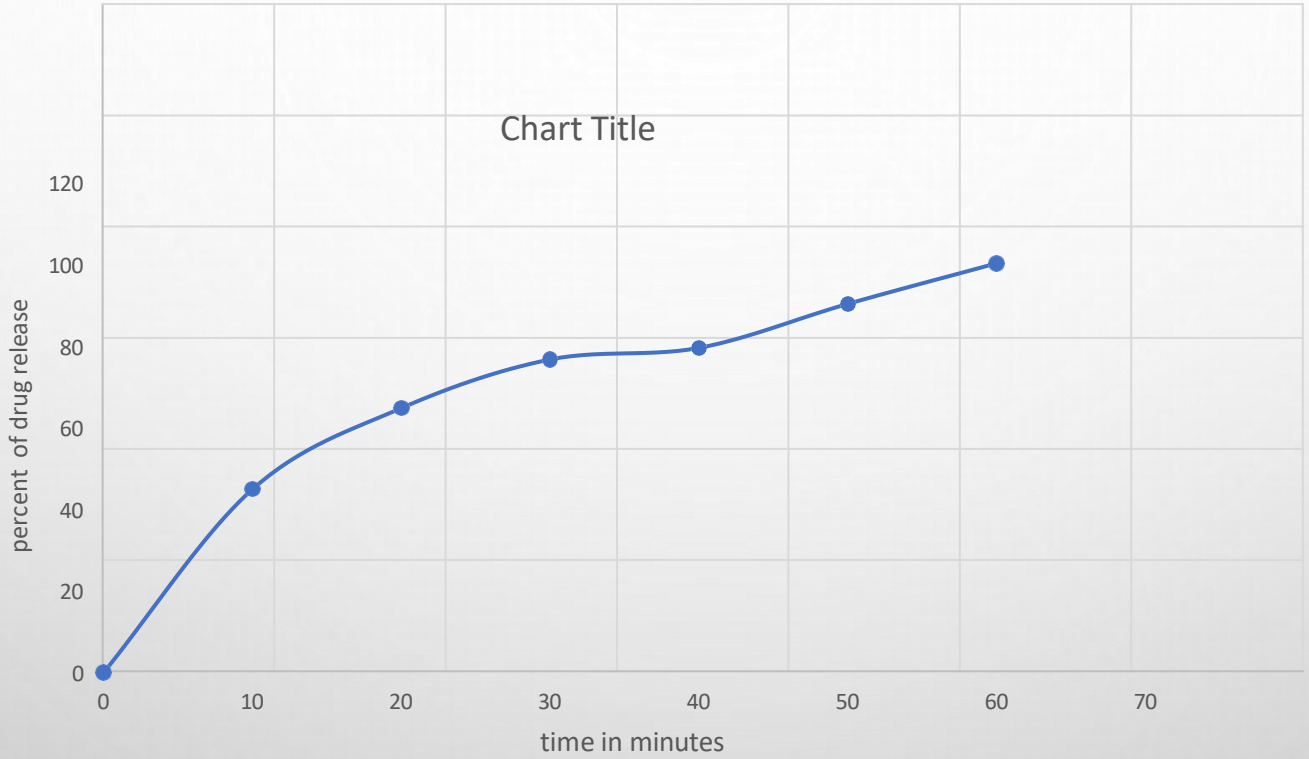


Chart Title
120
100
80
60
40
20
0
percent of drug release
0
10
20
30
40
50
60
70
time in minutes


thank you!