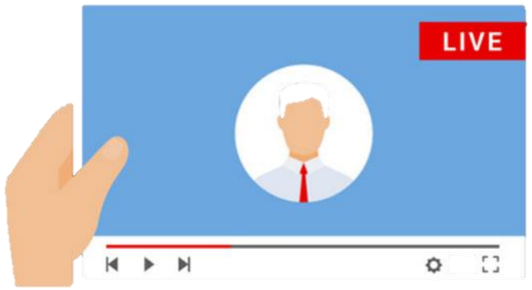


Welcome to GPAT

"Live online class"

Oral solid dosage form: Tablets 3

AIC. LMCP Foundation L.M College of Pharmacy Navarangpura, Ahmedabad - 380009

Agenda

Today's Topic: **Tablets – 3**

Recap

Evaluation of tablets

Tablets coating

Solve **5-6 GPAT Questions**

Recap

Introduction

Advantages and disadvantages

Formulation of Tablets: Excipients

Tablet formation machine: theory and operations

Methods of tableting

Types of tablets

11-12 GPAT Questions

Evaluation of tablets

Evaluation of tablets (I)

lists of tests

- Tablets are evaluated for their **physical, chemical and bioavailability properties**
- **Stability testing** is also an important evaluation parameter

Evaluation of tablets (I)

lists of tests

- Tablets are evaluated for their **physical, chemical and bioavailability properties**
- **Stability testing** is also an important evaluation parameter

Unofficial tests:

- Appearance
- Size and shape
- Organoleptic properties (color, odor, taste)
- Hardness
- Friability

Official tests:

- Drug content
- Weight variation
- Disintegration
- Dissolution

Evaluation of tablets (2)

Appearance, Size and shape and Organoleptic properties (color, odor, taste)

- Measurement of crown thickness: **Micrometer and Caliper scale**
- Tablet thickness values variations: **±5% variation** of a standard value

ORGANOLEPTIC PROPERTIES (T,C,O):

- Test for Taste, Color and odor for Patient Compliance

Quantitative color evaluation by;

1. **Micro-reflectance photometer (measure of color uniformity and gloss on tablet)**
2. **Tristimulus colorimetric measurement**
3. **Reflectance spectrophotometry**

Evaluation of tablets (3)

Friability

- This test is intended to determine, under defined conditions, the friability of uncoated tablets, the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition
- Laboratory apparatus known as **Roche friabilators** (made of plastic chambers) are used for the test.
- The drum is attached to the horizontal axis of a device that **rotates at 25 rpm**
- Usually, a sample of **10 tablets are tested at a time**, unless tablet weight is 0.65 g or less, where 20 tablets are tested. **After 100 turns (time?), the tablet samples are evaluated by weighing**

Evaluation of tablets (4)

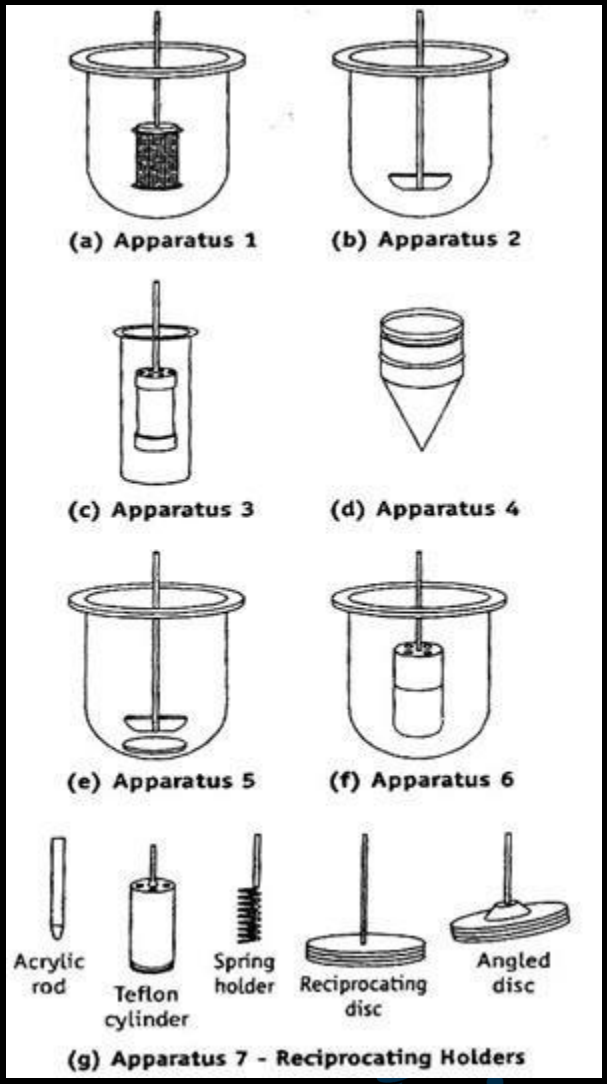
Friability

- Acceptable weight loss range :-- **<0.5-1%**
- **If cracked, cleaved, or broken tablets are obvious, then the sample also fails the test**

% F=(weight loss of tablets)/(original weight of tablets)*100

- **% of moisture content affects hardness and friability**
- **Rough handling tests :-- Vibration test, Drop test, Inclined plane test**
- **Webster & Van abbe tester indicate edge damage during handling**

Evaluation of tablets



Evaluation of tablets (5)

HARDNESS TESTING

- A tablet requires a certain amount of mechanical strength to withstand the shocks of handling in its manufacturing, packing, shipping, and dispensing
- **The need for testing hardness or crushing strength, in addition to friability, may be explained with an analogy that friability determines how fragile a tablet is**
- If a tablet is more fragile than expected, then the friability test will detect its substandard quality

Sr. No	Tester Name	Principle
1	Monsanto (Stokes)	Compressible spring between 2 plungers (manual)
2	Strong Cobb	By hydraulic pressure
3	Pfizer	Mechanical principle using a pair of pliers
4	Erweka	Same mechanical principle vertically
5	Schleuniger	Operates in horizontal position (most widely used)

Evaluation of tablets (6)

HARDNESS TESTING

- Tester 4 and 5 eliminates operation variability. It reads in both kg/cm² and strong cob unit kN

1 kg/cm² =10 kN

- Hardness of tablet depends on die fill and compression force
- **Vicker's test to measure surface hardness (Minimum requirement: -- 4 kg/cm²)**
- Certain tablets such as lozenges and buccal tablets intended to dissolve slowly are made hard

Evaluation of tablets (7)

Weight variation test

- The USP contains a test for determination of dosage form uniformity by weight variation for uncoated tablets
- In the test, 10 tablets are weighed individually and the average weight is calculated

Table: -- USP Weight Variation limits for uncoated tablets

Average weight (mg)	Maximum % difference allowed
<130	10
130 – 324	7.5
>324	5

Table: -- IP Weight Variation Limits for Uncoated Tablets

Average weight (mg)	Maximum % difference allowed
<80	10
80 – 250	7.5
>250	5

Uniformity in Diameter: --

<12.5 mm → +/- 5 % variation

>12.5 mm → +/- 3 % variation

Evaluation of tablets (8)

CONTENT UNIFORMITY TEST

- **Content of Uniformity in USP method:--**
  - By the USP method, 10 dosage units are individually assayed for their content according to the method described in the individual monograph
  - Unless otherwise stated in the monograph, the requirements for content uniformity are met if the amount of active ingredient in each dosage unit lies within the range of **85% to 115%** of the label claim and the **standard deviation is less than 6%**
  - If one or more dosage units do not meet these criteria, additional tests as prescribed in the USP are required **(If 9 tablets are in specification, then 10th must be not less than 75% or more than 125%)**
- Content of Uniformity in BP method
  - Take 20 tablets and range is **90%-110%**

Evaluation of tablets (9)

DISINTEGRATION TEST

- A disintegration test is a test to establish how fast a tablet disintegrates into aggregates and/or finer particles
- **Venderkamp disintegrator** tester is used
- The apparatus consists of a basket and rack assembly containing six open-ended transparent tubes **3 inch long (1 inch = 25.4 mm)**, held vertically upon a 10-mesh stainless steel wire screen
- During testing, a tablet is placed in each of the six tubes of the basket, and through the use of a mechanical device, the basket is raised and lowered in the immersion fluid at 29 to 32 cycles per minute, the wire screen always below the level of the fluid. Each tablet placed in each tube, basket position in 1 liter beaker of water at 37°C
- Tablet remains 2.5 cm below surface of liquid on upward movement and not close to 2.5 cm to bottom of beaker.

Evaluation of tablets (10)

DISINTEGRATION TIME OF DIFFERENT TABLET FORMS

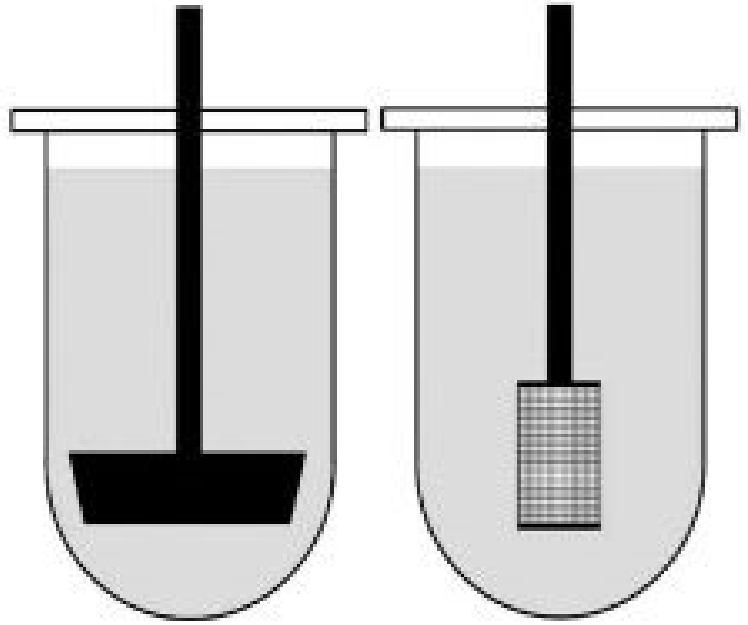
Sr. No	Tablet/Capsules	Liquid at 37 +/- 2 °C	Disintegration Time
1	Uncoated Tablets	Water	15 min
2	Coated Tablets (Sugar/Film)	Water / 0. 1 N HCl	60min
3	Enteric Coated Tablets	0.1 N HCl / Mixed phosphate buffer at pH 6.8	Not less than 2 hours
4	Vaginal Tablets	Water	30 min
5	Soluble, Dispersible and Effervescent Tablets	Water at 19-21 °C	3 min
6	Hard Gelatin Capsules	Water at 37 °C	30 min
7	Soft Gelatin Capsules	Water at 37 °C	60 min

Evaluation of tablets (I I)

DISSOLUTION TEST

USP Apparatus

- **Apparatus 1 (Basket)**:- For capsules, for dosage forms that tend to float or that disintegrate slowly.
- **Apparatus 2 (Paddle)**:- For tablets
- **Apparatus 3 (Reciprocating cylinder)**:-For bead –type modified-release dosage forms
- **Apparatus 4 (Flow cell)**:- For modified-release dosage forms
- **Apparatus 5 (Paddle over disc) & Apparatus 6 (Cylinder)**:- For evaluating & testing transdermal dosage forms
- **Apparatus 7 (Reciprocating disc)**:- For non-disintegrating oral modified-release & transdermal dosage forms



Evaluation of tablets (12)

DISSOLUTION TEST

Experimental Testing conditions:-

- **Dissolution medium –** deaerated water, buffered solution (pH- 4 to 8),dilute acid (0.001N to 0.1N HCl)
- **Volume of dissolution medium -** 500-1,000 ml (The quantity should be not less than 3 times that required to form a saturated solution of the drug substance)
- The **pH of the test medium -** within pH 1.0 - 6.8.
- **Speed**
  - 100 rpm (for apparatus 1-basket)
  - 50 rpm (for apparatus 2-paddle)
- **Temperature** - 37 ± 0.5 C

Evaluation of tablets (13)

DISSOLUTION TEST

Acceptance criteria:

Stage	Number Tested	Criteria
S1	6	Each unit is not less than 0 + 5%
S2	6	Avg. of 12 units (S1+S2) is equal to or greater than Q,& no unit is less than Q - 25%
S3	12	Avg. of 24 units (S1+S2 +S3) is equal to or greater than Q, NMT 2 units are less than Q- 15%, no unit is less than Q-25%

GPAT QUESTION

What is the disintegration time for film coated tablets?

A. 3 min

B. 15 min

C. 60 min

D. 120 min

APOMIND

GPAT QUESTION

Match the following

I. Apparatus 5	A. Paddle over disc
II. Apparatus 7	B. Reciprocating disc
III. Apparatus 3	C. Reciprocating cylinder
IV. Apparatus 6	D. Cylinder

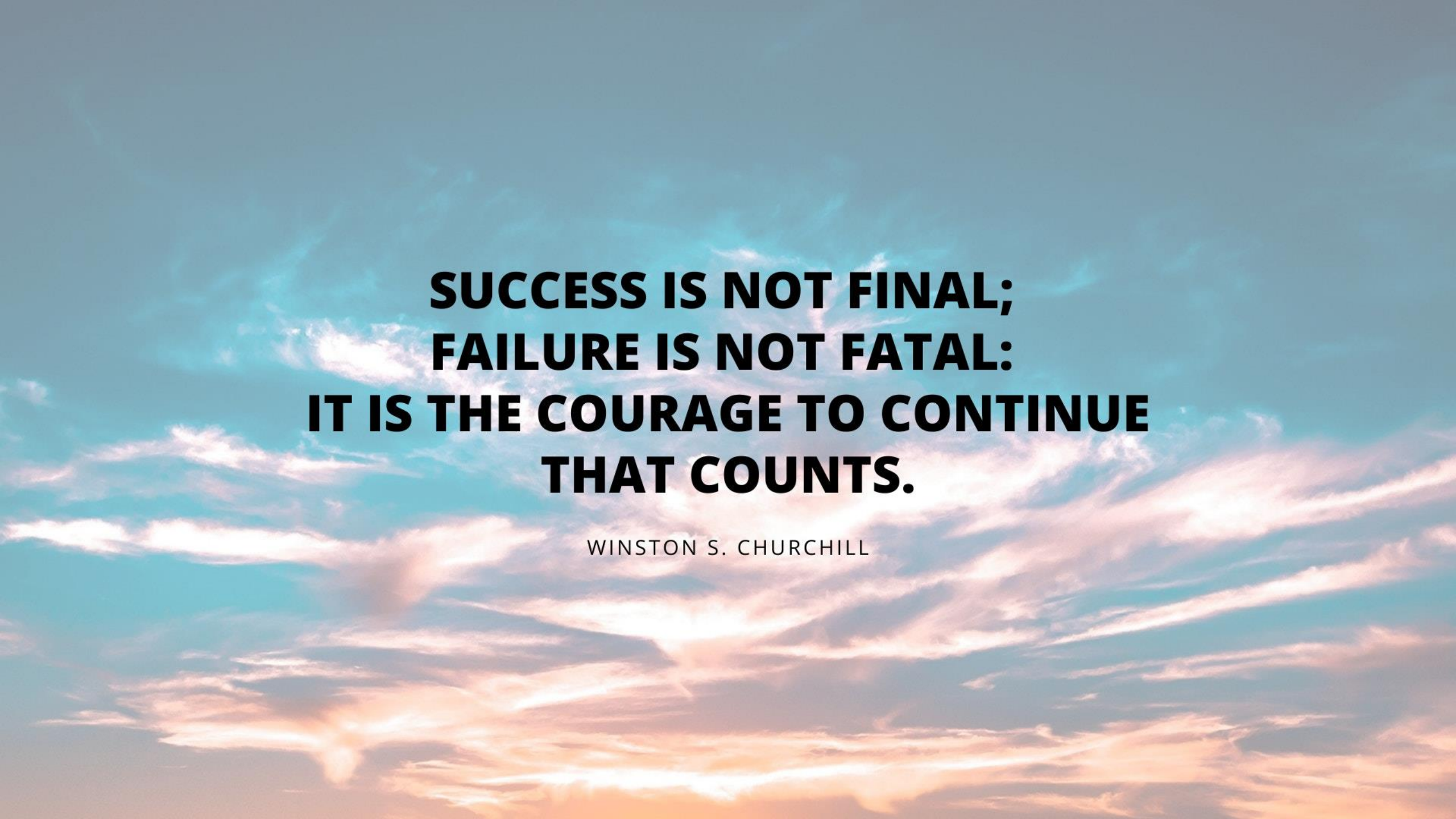
A. I→C; II→A; III→B; IV→D

B. I→A; II→B; III→C; IV→D

C. I→B; II→A; III→C; IV→D

D. I→C; II→B; III→A; IV→D

APOMiNd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FAILURE IS NOT FATAL:
IT IS THE COURAGE TO CONTINUE
THAT COUNTS.
WINSTON S. CHURCHILL

TABLET COATING

APOMIND

TABLET COATING

Why do we need to coat tablets

- Used to **mask taste, odor, and color to provide physical and chemical protection**
- To **control the release** of drug from tablet
- To **protect** the drug from **gastric environment** of stomach with acid resistant enteric coating
- **To incorporate another drug/formula adjuvant in coating to avoid chemical incompatibility and sequential drug release.**

TABLET COATING

Sugar Coating

- The sugar coating of tablets may be divided into the following steps:

  (a) Sealing

  (b) Subcoating,

  (c) Syrup coating/Color coating

  (d) Polishing

- Tablets intended to be coated are manufactured to be thin edged and highly convex to allow the coatings to form rounded rather than angular edges

- Sugar coating increase the **50-52% thickness of tablets**.

TABLET COATING

Sugar Coating -> Sealing

Sealing:

- **Water proof coating** because without it tablets would absorb excess moisture leading to tablet softening/disintegration
    - **Shellac**: It is mostly commonly used sealant but undergo aging due to polymerization resulting in lengthening or increase in tablet disintegration and dissolution time
    - **Zein**: Alcohol soluble protein derivative from corn is also effective sealant

TABLET COATING

Sugar Coating – Sealing → Subcoating

Subcoating:

- To **round the edges & build up the tablet size** (50%-52%)
- Sub coating steps consists of alternatively applying a **sticky binder (acacia/gelatin)** solution to tablets followed by a **dusting of sub coating (Talc, $CaCO_3$) powders** & then **drying**
- The process is **repeated** until desired thickness is achieved (3-4 sub coats)

TABLET COATING

APOMIND

TABLET COATING

Syrup coating/color coating:

- It is to **cover & fill the imperfections** in tablet surface caused by sub-coating step and impart desired color to the tablet
- This step requires most **skill person**
- The first syrup coats usually contain some suspended powders called as **grossing syrups**
- **No color** should be added until tablets become smooth

Polishing:

- It is done by powdered wax i.e. **beeswax or carnauba wax** or warm solution of these waxes in naphtha or suitable volatile solvents.

TABLET COATING

Film coating

- The film-coating process, which places a **thin, skin-tight coating of a plastic-like material over the compressed tablet**, was developed to produce coated tablets having essentially the same weight, shape, and size as the originally compressed tablet
- Film-coated tablets also are far **more resistant** to destruction by abrasion than are sugar coated tablets
- **Weight gain is only 2-6%**

TABLET COATING

Film coating

Film formers:

Non-enteric film formers →

- HPMC (Hydroxy propyl methyl cellulose);
- Ethyl cellulose;
- Povidone;
- Hydroxy propyl cellulose (HPC);
- Sodium carboxymethyl cellulose;
- PEG;
- Acrylate polymers or carbopol (Eudragit)

Enteric Coating Polymers →

- Cellulose acetate phthalate (CAP);
- Hydroxy propyl methyl cellulose phthalate (HPMCP);
- Polyvinyl acetate phthalate (PVAP);
- Acrylate polymers or carbopol (Eudragit)

TABLET COATING

Film coating → Non-enteric film formers

HPMC (Hydroxy propyl methyl cellulose):

- Mostly used

Alkali treated cellulose + CH_3Cl → Introduce methoxy groups → (propylene oxide) To introduce propylene glycol ether

- Mostly used
- Different grades are available depending upon the viscosity, generally low grades are preferred
- When used alone, the polymers have **tendency to bridge or fill the debased tablet surfaces**

TABLET COATING

Film coating → Non-enteric film formers

Ethyl cellulose:

- It is totally **water insoluble & GIT fluids polymer & pH independent so should not be used alone**
- It is mostly used for **delayed/sustained release tablets** in combination with water soluble additives

Povidone:

- It is **1-vinyl 2-pyrrolidinone**
- It also acts as **binder** & hence improves the dispersion of colorants in coating solution for uniformity
- **4 viscosity grades given by K values i.e. K-15 [10000], K30 [40000], K45 [160000] & K 60 [320000]**

TABLET COATING

Film coating → Non-enteric film formers

Hydroxy propyl cellulose (HPC):

- It is soluble in H_2O below 400 C & insoluble above 450 C
- It produces the **film extremely tacky**

Sodium carboxymethyl cellulose:

- Water soluble polymer easily dispersed in water to form colloidal solution but **it is insoluble in most of organic solvents.**

TABLET COATING

Film coating → Non-enteric film formers

APOMIND

PEG:

- **PEG – 200-600** molecular weight → **Liquid at room temperature** & used as plasticizer for coating solution filtrate.
- **PEG 900-8000** are **white waxy** solids at room temperature
- These polymers used in combination with other polymers to modify the film properties
  - **Combination PEG waxes + cellulose acetate phthalate (CAP) provides films are soluble in gastric fluids → used for non enteric coating process**

TABLET COATING

Film coating → Non-enteric film formers

Acrylate polymers or carbopol:

Dimethyl aminoethyl methacrylate + methacrylic acid ester

- **Eudragit E (cationic polymer)** → is only Eudragit material that is freely soluble in gastric fluid up to pH 5
- **Eudragit RL & RS** → pH independent polymers so for delayed release
- **Eudragit E** → non enteric coating
- **Mostly these polymers are available in isopropanol solvents**

TABLET COATING

Film coating → Enteric Coating

Enteric Coating

- Mostly esters of phthalates → protect acid-labile drugs from gastric fluid e.g. enzymes and antibiotics, to prevent the gastric distress e.g. sodium salicylate, to deliver the drugs intended for local action in intestine. E.g. Shellac, phalates & Eudragit L & S
- **The pH of stomach contents varies from pH 1.5 - 4**
- The pH of the material approaching pylorus (last part of stomach) is nearly 5 → An ideal enteric polymer should dissolve or become permeable near and above pH 5
- The above pH these polymers with **CAP, HPMCP, Polyvinyl, acetate phthalate** [which are dicarboxylic acid + pthalic acid] in partially esterified form starts to lose their film integrity due to ionization of carboxylic group on chain and subsequent hydration
- Further, the presence of esterases in intestinal fluid breakdown ester linkage of polymer chains

TABLET COATING

Film coating → Enteric Coating

Cellulose acetate phthalate (CAP):

- Dissolves **above pH 6**, it is hygroscopic, films are brittle, usually formulated with hydrophobic film (to prevent hygroscopic) forming material for better enteric films
- Aqueous enteric coating called as **AQUATERIC**, used with colloidal dispersion of latex particles + CAP

HPMCP:

- **Hydroxy propyl methyl cellulose phthalate**
- **HPMC + Pthalic anhydride → HPMCP**
- **Dissolves at pH 5-5.5 (pylorus pH)**

TABLET COATING

Film coating → Enteric Coating

APOMIND

Polyvinyl acetate phthalate (PVAP):

- Supplied as ready to use or ready to disperse enteric systems.

Acrylate polymers:

- **Eudragit L → Soluble at pH 6**
- **Eudragit S → Soluble at pH 7**

TABLET COATING

APOMIND

TABLET COATING

Solvents

- **To dissolve or disperse the polymers & other additives**
- Small concentrations of polymers i.e. **2-10%**
- Should **not** result in **extremely viscous solution system** i.e. > 300 cps, it should have **rapid drying rate** i.e. the ability to coat 300 kg load in 3-5 hrs.
- **Water** → Drugs can hydrolyze, increase in viscosity of coating solution or the drug must require initial seal coat with non aqueous solvent based coating
- **Others (Organic):** Isopropanol, Acetone, Ethanol, Methanol, Methyl ethyl ketone.

TABLET COATING

Plasticizers

Isothermal plasticizing technique:

- It is the chemical modification of basic polymer that alters the physical properties of the polymer

  E.g. degree of substitution, type of substitution, chain length etc. polymer properties are varied

External plasticizing techniques:

- Here a plasticizer is added to achieve desired effects. The external plasticizer can be non-volatile liquid or another polymer which when incorporated with the primary polymeric film former, changes the flexibility, tensile strength or adhesion property of the resulting film
- Plasticized range from **1-50% by weight** of a film former
- **Commonly used plasticizer are – castor oil, PEG 200 – 400 and surfactants like polysorbates (tween), sorbitan esters (spans)**
- For aqueous coating mostly water soluble plasticizer used are PEG & PPG (poly propylene glycol) Castor oil & spans are used for organic solvents based coating solutions.

TABLET COATING

Colorants and Opaquant

Colorants:

- To achieve proper distribution of suspended colorants in coating solution requirement uses of **fine powdered colorants < 10 µ**
- Lakes are dyes absorbed on $Al(OH)_3$ or talc become choice for sugar and film coating systems
- **Natural coloring materials:** anthocyanin, caramel, carotenoids, carminic acid, indigo, flavones
  - **Opalux — Opaquant color concentrate for sugar coating**
  - **Opaspray — Opaque color concentrate for film coating**
  - **Opadry — Complete film, coating concentrate.**

TABLET COATING

Colorants and Opaquant

Opaquant:

- These are **very fine inorganic powders** used in the coating solution formulations **to provide more pastel colors and increase film coverage**

- Colorants are much more expensive than these inorganic materials, and effectively less-colorant is required
- **Provide white coating or more pastel colors. E.g. Titanium dioxide (TiO_2), Talc, $Al(OH)_3$**

GPAT QUESTION

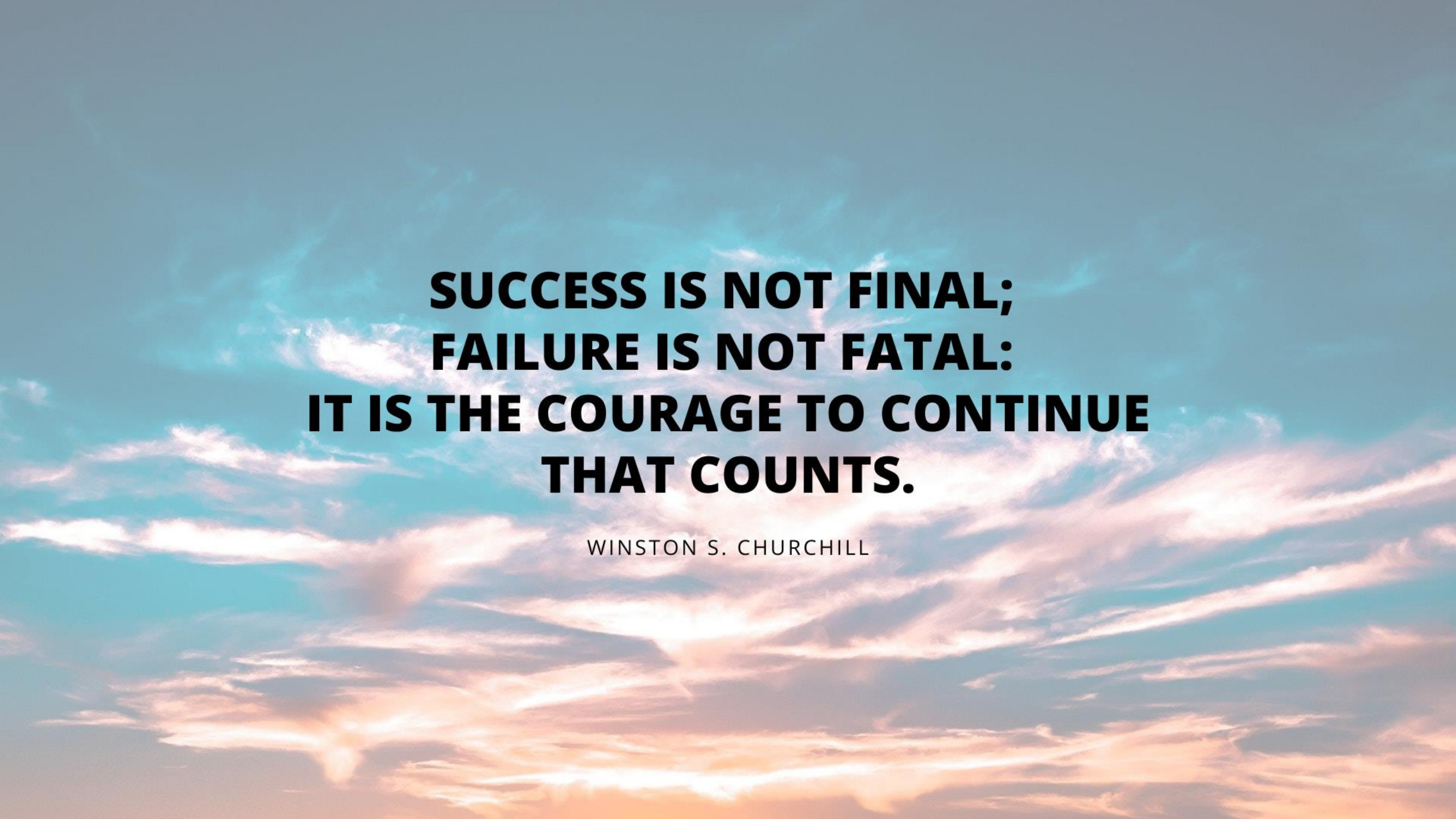
Subcoating is given to the tablets to

A. Prevent dissolution in acidic medium

B. Round the edges and build up the tablet size

C. Prevent moisture penetration in to the tablet

D. Avoid deterioration due to microbial attack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