Toppersnotes
Unleash the topper in you

GPAT

GRADUATE PHARMACY APTITUDE TEST

NATIONAL TESTING AGENCY (NTA)

VOLUME – 2

PHARMACUETICS, PHYSICAL ANALYSIS & MICROBIOLOGY

SIERRA INNOVATIONS

CONTENT

PHARMACEUTIC

1.	**Classification of dosage form**	1
2.	**Tablet**	1–16
3.	**Capsule**	17–21
4.	**Microencapsulation**	22–24
5.	**Semisolid**	25–27
6.	**Suppositories**	28–29
7.	**Sterilization**	30–34
8.	**Filtration**	35–38
9.	**Sterile product**	39–43
10.	**Ophthalmic product**	44–46
11.	**Aerosole**	47–49

BIOPHARMACEUTICAL & PHARMACOKINETICS

12.	**Biopharmaceutics**	50–52
13.	**Kinetic & drug Stability**	53–55

14. **Biopharmaceutical Classification System (BCS)**	55–56
15. **Dissolution Test**	56
16. **ICH**	56–57
PHARMACEUTICAL JURISPRUDENCE	
17. **Drug & Cosmetic Act**	58–59
18. **Pharmacy Act (All)**	60–68
PHYSICAL PHARMANCY	
19. **Micrometrics**	69–74
20. **Surface interfacial Tension**	75–79
21. **Rheology**	80–88
22. **Dispersion System**	89–92
23. **Suspension**	93–97
24. **Emulsion**	98–102
25. **State of Matter**	103–104
DISPENSING PHARMACY	
26. **Prescription**	105–106
27. **Posology**	106

28. **Incompatibility**	107–108
29. **Pharmaceutical Calculation**	109–110
PHARMACEUTICAL ENGINEERING	
30. **Distillation**	111–112
31. **Heat process**	113–114
32. **Size Reduction**	114–118
33. **Extraction**	118
34. **Mixing**	119–122
MICROBIOLOGY	
35. **Bacteria**	123–131
36. **Virus**	131–135
37. **Fungi**	136–137
38. **Test for Sterility**	137–138
39. **All Subject Some Important Topics & Questions**	139–187

Classification of Dosage form

1. Solid dosage form:-
   - Tablet
   - Capsule
   - Powder
   - Granule
   - Lozenges → Unit solid dosage form
2. Liquid Dosage Form:-
   - Syrup
   - Mouthwash
   - Elixir
   - Linctus

   } Monophasic
   - Suspension
   - Emulsion

   } Biphasic
3. Semi Solid Dosage Form:-
   - Cream
   - Paste
   - Gel
   - Ointment
4. Gaseous Dosage Form :-
   - Aerosole
   - Inhalers

Tablet

* Tablet is a unit dosage form that is prepared by either compression or molding method.
* It contain drug substance with or without suitable diluent.
* Diluent:- Other than active drug substance is called Diluent.

Type of tablet

1. Tablet Ingested Orally:
   * Compressed Tablet
   * Multiple Compressed Tablet

* Enteric Coating Tablet (For Delayed action)
* Sustained Action Tablet (For Controlled released tablet)
* Sugar Coated Tablet
* Film Coated Tablet
* Chewable Tablet

2. Tablet used in orally (cavity):-

e.g:- (A) Buccal Tablet → Placed inside of check

* Absorbed Directly into Buccal cavity.
* By bass first pass metabolism e.g. Progesterone.

(B) Sublingual Tablet

* Sublingual tablet placed under the tongue.
* E.g:- Nitroglycerin, Erythrityl Tetra nitrate.

(C) Troches & Lozenges

* Produced local effect in mouth or throat.
* E.g:- Local Anesthetic, Antiseptic, Anti-bacterial Agent

(D) Dental Cone

* Compressed tablet placement in the empty socket after tooth extraction.
* Dissolve in 20-40 minute.

3. Tablet placed by other Route:-

E.g:- (A) Implantable tablet

* Inserted subcutaneously by kern injector.
* For Controlled Release action. Like 1 month to 1 year or more.
  e.g.:- contraceptive or other hormonal drug.

(B) Vaginal Tablet

* These type of tablet inserted into vaginal cavity.
* E.g:- Antibiotic etc.

4. Tablet used to prepare Solution:-

E.g:- (A) Effervescent Tablet

* It contain effervescing agent like sodium carbonate, Citric acid or tartaric acid.
* They produce a solution rapidly with release of Co_2 like ENO (ENO is a Effervescent powder) But Effervescent tablet are available in the from of tablet

(B) Dispensing Tablet:-

* They are concentration form of tablet, injected before dilution.
* Added a given volume of water or produce solution.
* E.g:- Silver Compound
* Quaternary ammonium Compound.

(C) Hypodermic Tablet:-

* Diluted with sterile water.
* Injected Parentally
* Hypokalemic Tablet + Sterile Water (injected).

(d) Tablet Triturate:-

* Diluted with inert solid substance.
* Tablet Triturate (Active ingredient) + inert substance like lactose, or dextrose etc.

Tablet Ingredients

Tablet Contain → Active Ingredient (Produce action)
→ Inactive Ingredient/Excipient/Additive

Additive:- Additive impart satisfactory processing, compression (Characteristic, give additional physical property, or give controlled release action.)

E.g:- - Diluents,
- Binder,
- Disintegrate,
- Glident,
- Lubricant,
- Coloring agent- give color,
- Flavors,
- Sweetening agent- Coat unpleasant test,
- Polymer & wax (for controlled action)

Diluent:-

* Used to increase bulk of tablet
* Diluent are filter.
* Diluent can be used up to 80□ of the total weight of tablet.

Important:- All sugar contain diluents have tendency to undergo reaction drugs containing-NH_2 group. This is called mallard Reaction.

Calcium phosphate as diluent reduces bio availability of some antibiotic like tetracycline.

Type of Diluent:-

1. Sugar → :- Dextrose
   - Lactose, (Cause miliary Reaction)
   - Sucrose
   - Manitol
   - Sorbitol
2. Polysaccharilce → Starch , Cellulose
3. Inorganic Compound → - Calcium Carbonate
   - Calcium Phosphate
   - Magnesium Carbonate
4. Other → - Bentonite
   - Kaolin
   - Silicon Derivative

Lactose:- Lactose is widely used diluent. It have good compressibility. They are available in the form of;

1. α –Lactose (Hydrous)
2. β- Lactose (Anhydrous)
3. Spray dried Lactose

Lactose Disadvantage:- Cause Millard reaction with amino group

Millard Reaction:- Lactose + Amino group drug + Alkaline lubricant (Mg stearate)

↳ Tablet discolor (Due to formation of formaldehyde)

* **Mannitol**:- used in chewable tablet due to negative heat of solution, cooling effect.
  * Mannitol is non-hygroscopic

    * Non Carcinogenic
* Sorbitol is optical isomer of mannitol.
* Sucrose:- (Table sugar)
    * It is a hygroscopic in nature.
    * Used as direct compression tablet.
    * As binder.
    * As bulking agent.
    * Also used as sweetener in chewable tablet.

Important:- Sugar tab.:- 90-93% Sucrose + 7-10% invert sugar

Dipac :- 97% Sucrose + 3 % invert sugar

Nutab:- 97% Sucrose + 4 % invert sugar

* Sucrose $\xrightarrow{\Delta\, H_2O}$ Invert sugar (Glucose + Fructose)
* Starch :- Directly compressible starch
    ↳ Sta Rx 1500
    * Hydrolyzed Starch ⟶ Emdex Celutab.

* Granulating Agent:- used to convert the fine powder into grannies.
    E.g:- Water, starch, Mucilage, Tragacanth, Alcohol, Acetone.
* Binder:- used to provide cohesive qualities
    * More the binder, harder the tablet
    * Type:- (i) Solution Binder (E.g:- Starch, sucrose, gelatin, acacia, tragacanth)
    * (ii) Dry Binder (E.g:- Cellulose Derivative, Cross linked PVP)
* Lubricant:- Reduce fraction between wall of tablet & wall of die during tablet ejection.
* Anti-adherent:- Present adhesion of the tablet material to the surface of dies& Punchers.
* Glidant:- Reduce inter-particle friction & improve the rate of flow of tablet granulation
* Lubricant:- Calcium Stearate, Magnesium Stearate
* Anti-adherent:- Excellent ⟶ - Talc (1-5%)
    * Corn Starch (5-10%)
    Good - Calcium stearate, Magnesium Stearate
* Glidant:- Excellent ⟶ - Corn Starch , Colloidal Silica

Good - Talc (1-5%)

* Disintegrate:- Facilitate breaking up to tablet in contact with water GIT.
  By two Method
  1. By swelling :- Alginate , starch der. PVP
  2. By wetting :- SLS, Clay, Bentonite, Veegum (Mg. aluminum silicate)

* Super disintegrate example:- Cross caremelose ⟶ Cross linked Cellulose
  - Crospovidone → Cross Linked PVP
  - Sod. Starch glycolate → Cross linked starch

* Sweetening Agent :-
  1. Mannitol → 72 Times sweetener than sugar
     - Used in chewable tablet
  2. Saccharine → 500 Times sweetener than sugar
     - Carcinogenic
  3. Aspartame → 200 times than sugar
     - Non- carcinogenic

* Aspartam is a methyl ester of the aspartic acid/phenyl alanine dipeptide.

Manufacturing of tablet

1. Preparation of granule for compression
2. Compression of granule into tablet
3. Coating of tablet
4. Evaluation of tablet

1. Preparation of Granule for Compression :-

Weighing the Ingredient

↓

Pulverization & Mixing

* In this step solid powder ingredient are reduced to the same size.
* Done to protect from segregation during mixing

↓

Convention of mixed

There are three method for formation of granule:-
1. Wet granulation
2. Dry granulation

3. Direct Compression

1. **Wet Granulation Method** :-

Drug + Diluent

↓

Dry Binder is added

↓

Blended uniformly

↓

Suitable Solvent is added

↓

Blended till wet mass formed

↓

Wet Screening

↓

Drying (By tray dryer or fluid bed dryer)

↓

Dry Screening (Particle size reduced)

↓

Lubrication & Compaction

↓

Tabled formed

2. **Dry Granulation step**:- It apply when the product is sensitive to heat e.g. Aspirin, vitamin.

Process:-

Milling

↓

Mixing

↓

Screening

↓

Blending

↓

Slugging

↓

Screening

↓

Granulation

* Slug :- Described as compact mass of powder.

3. Direct Compression:- Uses directly compressible diluent like spray clerical lactose.

Process:-

Weighing

↓

Mixing

↓

Screening

↓

Compression

E.g.:- NaCl, KCl, Can be directly compressed.

Advantage of preparation of Granule:- Simple powder may not have desired flow property but after granulation, powder, material are improved by forming shape aggregate called granule→ Having good flow property & prevent segregation.

Part of tablet machine

1. Hopper:- For holding & Feeling granulation to be compressed.
2. Dies:- Define the size & shape of the tablet
3. Punches:- Used for compression of granulation with the die.
4. Cam track:- Guide the movement of the punches
5. Turrets:- Hold upper & lower punches
6. Feeling machine:- Used for moving granulation from the hopper to the die.
7. Die table:- Portion holding the dies.

Defect of Tablet

1. Capping:- Partial or complete separation of top or bottom crown of tablet
2. Lamination:- Separation of tablet into two or more distinct layer.

   Capping & Lamination problem are due to:-

   * Air Entrapment
   * Deep Concave Punches
   * Dry Granulation

   Both problem corrected for:-
   * Pre Compression
   * Using flat punches, slowing tableting rate.
   * Add certain % of moisture by e.g. sorbitol, MC, PEG etc.

3. Picking:- Material adhere to punch faces
   Sticking:- Material adhere to the die wall, occur due to excessive moisture.

   Both problem corrected for:-
   * Proper drying of granule
   * Plating of punch face by→ Chromium

4. Mottling:- Non-uniformity of color over the tablet is called mottling.
5. WT variation:- Occur due to poor flow, lack of glidant, lack of sufficient lubricant, bridging etc.
6. Double impression:- Due to uncontrolled movement of punch. Correct by using anti turning device.
7. Hardness variation:- Due to weight variation in granule filled in die.
   Corrected by using proper tooling machine.

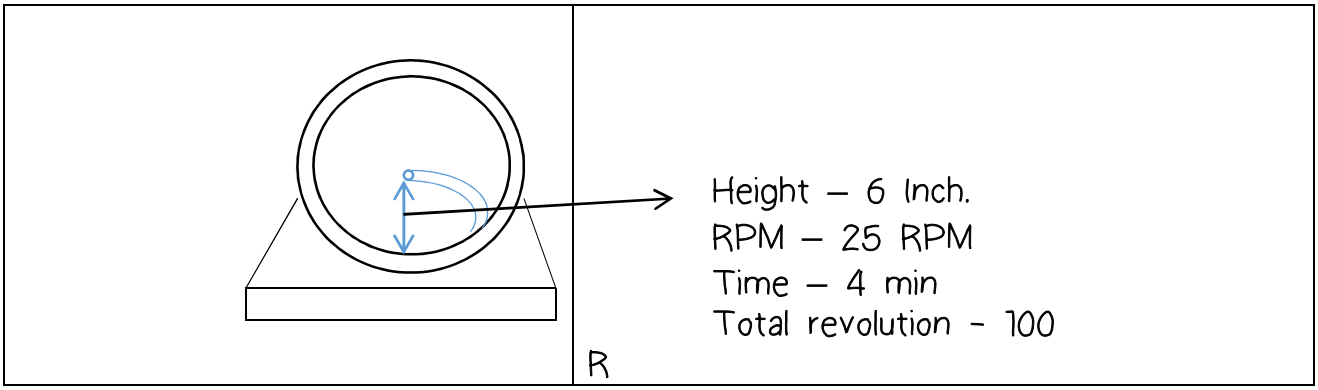
Evaluation of tablet

1. Size & shape:-
   * Crown thickness of tablet measured by micrometer.
   * Total crown thickness is measured by vernier caliper.
   * Tablet thickness should be controlled with ±5% of standard value.

2. Hardness of tablet:-
   * It is force required to break the tablet in diametric compression test.
   * Hardness of tablet affect dissolution behaviors (more hard the tablet, More time taken during dissolution).
   * Hardness also called crushing strength.
   * Standard hardness should be minimum 4 Kg.

   Device used:-
   I. Monsanto tester:- Give Strength in 4 Kg.
   II. Strong cobb tester:- Force applied by hydraulic pressure & later air pressure.
   III. Pfizer tester:- Force applied by hydraulic pressure & latter air pressure.
   IV. Erwaka tester:- Gives strength in kg.

3. Friability:- Friability is useful for determination of drug loss during transportation & its is determined by Roche friabilator.



   * Tablet fall from → 6 inch distance
   * Speed → 25 RPM
   * Time → 4 min
   * Total Revolution → 100
   * % Acceptance :- Not more than 1% (I.P)
   * 0.5 to 1% (USP)
   *

$$\% \text{ Friability} = \frac{Initial\ WT - Final\ WT}{Initial\ WT} \times 100$$

Whispering gives high friability value.

4. Uniformity of WT (Weight variation):-

* Total tablets used for the test → 20
* 20 tablet selected randomly & calculate the average wt.

Average weight of tablet		Maximum % of difference allowed
IP	USP	
80 Mg or loss	130 Mg or less	± 10%
80-250 Mg	130-324 Mg	± 7.5%
More than 250 Mg	More than 324	± 5%

5. Uniformity of content:-

* Total tablet taken - 30
* Total assayed – at least 10 → by analytical technique
* Total passed if

  ↳ Nine of the tablet should contain 85-115% (or 100 ± 15%) content & 10th tablet may contain 75-125% (or 100 ± 25%) content.
* If above condition not satisfied than other 20 tablet should be assayed & no one should fall outside 85-115% or 100± 15% range.

6. Disintegration Test:-

* It is not applicable to modified release or mouth dissolving tablet.

Apparatus:- Tablet Disintegrator.

* Tablet → 6 (selected randomly)
* Glass tube →6
* Glass tube length → 3 inch.
* Mess screen → 10 mesh → 1.7 mm (USP)
* 8 mesh → 2mm (IP)
* Upper & lower end closed with 10 mesh screen.
* Beaker contain → 900ml of water simulated gastric fluid or simulated intestinal fluid.
* Temperature:- 37 ± 2%
* Speed → 28-32 RPM
* Limit of Disintegration Test IP/USP

S.No	Tablet/Capsule	Liquid (Medium)	Disintegration
1	Dispersible & Effervescent tablet	Water (19-21°C)	3 min
2	Uncoated tablet	Water	15 min (30 min USP)
3	Film coated	Water or 0.1 N HCl	30 min
4	Sugar coated	Water	60 min
5	Enteric coated tablet	0.1 N HCl with phosphate buffer	2 hr in gastric fluid media & 1 hr in intestine fluid media
6	Hard Gelation	Water	30 min
7	Soft Gelation	Water	60 min

7. Dissolution Test:- According to USP for solid dosage form (tablet & capsule) dissolution apparatus used are:-

S.No	USP Apparatus	Type	Uses
1	Apparatus – I	Rotating Basket	Capsule, modified release solid dosage form
2	Apparatus – II	Paddle	Tablet, modified, release solid dosage form
3	Apparatus- III	Reciprocating	Determination of pH Profile of modified release dosage from.
4	Apparatus –IV	Flow through cell	Rapid degradation drugs
5	Apparatus –V	Paddle over disc	Transdermal patch, ointment, emulsion
6	Apparatus-VI	Rotating cylinder	Transdermal Patch
7	Apparatus –VII	Reciprocating disc	Transdermal patch.

Dissolution apparatus Comparison

USP apparatus - I → Basket

USP apparatus - II → Paddle

IP & BP apparatus - I → Paddle

IP & BP apparatus – II → Basket

Dissolution test Vs. Disintegration test

S. No.	Variable	Disintegration	Dissolution
1	Mesh screen of the bottom end of the basket	10	40
2	Temperature	37 ± 2°C	37 ± 0.5°C
3	Speed	28-32 RPM	50-70 RPM
4	Tablet remain below the surface of the liquid & descend not closer than	2.5 cm (25mm)	2.3-2.7 cm (23-27 mm)
5	Medium (pH 7.4)	900ml	900ml

Tablet coating

Type of coating :- 1. Sugar coating
2. Film coating
3. Enteric coating
4. Specialized coating

1. Sugar coating:-
Steps of sugar coating:-

Sealing
↓
Sub coating
↓
Smoothing (Syruping)
↓
Color coating
↓
Polishing
↓
Printing

Objective of coating:-

1. To mask taste, odor, color of the drug.
2. To provide physical & chemical protection to the drug.
3. To control release of the drug from the tablet.
4. To protect drug from gastric environment e.g. enteric coated tablet.
5. To avoid chemical incompatibility.
6. To provide physical elegance.

1. Sugar coating:-
   1. Seal coating (Sealing):- to prevent moisture penetration into the tablet core
      ↳ Shellac is a effective sealant tablet disintegration & dissolution time tend to lengthen on aging because of the polymerization of the shellac.

      * Zein has also been used as another effective sealant which does not lengthen tablet disintegration & dissolution time.

   2. Sub coating:- Sub coating is applied to round the edge & build up tablet size.
      * Sugar coating can increase the weight by 50 to 100%.

   3. Smoothing (Syruping):- To cover & fill imperfection in the tablet surface caused by sub coating step.
      e.g:- simple syrup solution (Glossy syrup), corn starch.

   4. Color coating :- to impart elegancy & uniform color.

   5. Polishing:- provide desired lusture on the surface of tablet.
      e.g:- Beeswax, paraffin, carnauba wax.

   6. printing :- By mean of a process of offset rotogravure.

2. Film Coating:- An ideal film coating material should have the following attributes:-

* Solubility required for the intended use e.g. free water solubility or pH dependent solubility (enteric coating)
* Capacity to produce an elegant looking product.

* stability in the presence of heat, light, moisture, air & the substrate being coated. The film property should not change with age.
* Essentially no color, taste or odor.
* Compatibility with common coating solution additives.
* Film coating (add 2 to 5 % to the tablet weight) done by three methods:-
  1. Pan pour method
  2. pan Spray method
  3. Fluidized bed press (Air suspension coating)

Material used in film coating

Non Enteric Material

* HPMC (Hydrolyze, propyl methyl cellulose)
* Ethyl cellulose
* PVC (Polyvinyl pyrrolidone)
* PEG (Poly ethylene glycol)

3. Enteric Coating:-

* To resistance to gastric acid.
* Ready susceptibility to or permeability to intestinal fluid.
  Enteric coating material (- phthalate)
* HPMCP (HPMC phthalate)
* Cellulose acetate phthalate
* Polyvinyl acetate phthalate
* Most common diluent used in tablet – Lactose (Milk sugar)
* Millard reaction (Drug having amino group, nitro group & metal show Millard reaction) with which diluent – Lactose
* Sta RX- 1500 is a trade name of – Starch
* Avicel – MCC (Micro crystalline cellulose)
* Aqua coat – 30 % Ethyl cellulose in alcohol
* Emcopress – Calcium hydrogen phosphate
* Ac-di-sol – Internally cross linked form of sodium CMC.
* Cerelose – Dextrose
* Cab-o-sil – Colloidal silica → Glident (used as polishing agent)
* Diluent having disintegrating properties – MCC
* Most commonly used binder or tablet manufacturing – Starch paste (10-20%)
* Substance increase the flow properties of granular is called – Glident
* Most commonly used glident – Talc (5%)