PARENTERALS

STORAGE CONDITIONS

STORAGE CONDITION	MEANING
Cold storage or under refrigeration	Usually 2 to 8 degree C.
Cool storage	Betⁿ. 8 to 25 °C.
Room temperature	20 to 25 °C
Warm	Betⁿ. 30 to 40 °C
Freezer	store betⁿ. -5 to -20 °C

IP TERMINOLOGY FOR SOLUBILITY

DESCRIPTIVE TERM	APPROXIMATE VOLUME OF SOLVENT IN ml/gm OF SOLUTE.
Very soluble	Less than 1 part
Freely soluble	1 to 10 part.
Soluble	10 to 30 parts.
Sparingly	30 to 100 parts.
Slightly	100 to 1000 parts.
Very slightly soluble	1000 to 10,000 parts.
Practical in-soluble	More than 10,000

WATER :- Commonly used vehicle for drug solⁿ.

TEST FOR QUALITY OF WATER
- A Gravimetric method.
- Electrolytic measurement of conductivity

TYPE	METHOD OF PREPARATION	COMMENT
WFI	Distillation or reverse osmosis	Not sterile, used within 24 hrs./stored below 2°C to 30°C
Purified Water	Distillation & ion exchange	Pharmaceutical solvent
Sterile WFI	Distillation or reverse osmosis	single dose container.
Bacteriostatic WFI	Distillation or reverse osmosis	Multiple & single dose.

NOTE :- Total solid content in WFI is 10 ppm / Sterile WFI is 20 to 40 ppm
Conductivity of WFI, should not more than 1 microohm^{-1}.

ROUTES OF ADMINISTRATION

ROUTE	SITE & QUANTITY	EXAMPLE
SC	Under skin layer	Insulin.
ID / IC	into dermis layer vol. 0.1 to 0.2 ml	Tuberculin skin testing etc.
IV	into vein, volume upto 500 ml.	Only aqueous preparation.
Intrathecal or Intra-spinal	into CSF or spinal cord vol. less than 20 ml.	spinal anaesthetic & antibiotics.
Intra-arterial	into artery	Antineoplastic drugs
Intra-articular	directly into joints	Antibiotics. Morphine, steroids.

TYPES OF PARENTERAL PRODUCTS

TYPE	VOLUME
Small Vol. Parenteral (SUV)	Vol. < 100 ml or equal to 100 ml
Large Vol. Parenteral (LUV)	Vol. > 100 ml.
Single dose container	size is limited to 1000 ml
Multiple dose container	size is limited to 30 ml

PARENTERALS

FORMULATION OF PARENTERALS

VEHICLE	EXAMPLE
Aqueous Vehicle (Water)	NaCl injection, Ringer solution, dextrose solution, Lactated - ringer solution.
Water miscible	Ethyl alcohol, Propylene glycol, PEG 300, 400, 600, Glycerine.
Non-aqueous	Fixed oil – ethyl oleate, isopropyl myristate etc

ADDITIVES :- Anti-micro bacterial preservatives

Ex :- Phenyl mercuric nitrate, phenyl mercuric acetate, methyl paraben, propyl paraben, Benzyl alcohol, phenol, chlorobutanol

ANTIOXIDANTS	EXAMPLES
1. Reducing agents (by oxidizing itself)	Ascorbic acid, Sodium bisulphite, Sodium metabisulfite, Thiourea.
2. Blocking agents. (block oxidative chain reaction)	Ascorbic acid esters, Butyl hydroxyl toluene (BHT), Butyl hydroxyl anisole (BHA), Nor dihydroguleretic acid (NDGA), Tocopherols.
3. Synergists - (Increase effectiveness of other antioxidants.	Ascorbic acid, citric acid, Tartaric acid, phosphoric acid.

4. Chelating agents – forms complexes & inactivate metal those are responsible for oxidative degradation of drug

Ex :- EDTA, Disodium edentate, Disodium ca. edentate

BUFFERING AGENT – USED IN CONC^{n} OF 0.1 to 5 %.

EX :- Acetic acid, Adipic acid, Benzoic acid, Citric acid.

- **Tonicity adjusters** – NaCl, Mannitol.
- **Stabilizers** – Glycine, Niacinamide.
- **Emulsifying agent** – Lecithin
- **Suspensing agents** – Gelatin, Pectin, Methyl cellulose, PEG – 4000

HEPA (high efficiency Particulate Air) filter –

→ Removes out particles of 0.3 microns.

→ Air velocity – 100 ± 20 ft/min.

Efficiency is checked by ★ Bubble point ★ DOP test

Freeze – Drying (Lyophilization)

→ When drug is unstable in sol^{n} form or thermolabile.

→ Generally F.P – 50 °C (should be done below the product collapse temperature)

PARENTERALS

CONTAINERS USED FOR PARENTERALS ARE :-

★ GLASS CONTAINER

Type	Description	Test	General Use
I	Highly resistant, borosilicate glass	Powdered glass	Buffered & unbuffered aq. sol^n, sterile product
II	Treated soda lime glass	Water attack	Buffered aq. sol^n below PH 7, dry powder & oleaginous sol^n.
III	Soda lime glass	Powdered glass	Dry powder and oleaginous solution.
IV	General purpose soda lime glass	powdered glass	Not for parenterals.

★ PLASTIC CONTAINER

Type	Uses.
Poly-propyline	Widely used due to high M.P
Poly-ethylene	Opthalmic products
Polystyrine	Plastic syrinches
Flexible PVC	Bags for I.V solution
Nylon & silicon rubber	I.V catheters

★ RUBBER CLOSURE

Type	Example
Elastomer	Natural rubber, Butyl rubber, Neoprene.
Vulcanizing	Sulfur.
Accelerator	2-mercaptobenzothiazole
Activator	ZnO, stearic acid
Filler	carbon black, clay Lime stone.
Antioxidant	Dilauryl thiodipropionate

★ DEVICES USED

→ I.V catheters - Nylon & silicon
→ Hypodermic needle - stainless steel

★ PYROGENS

→ these are lipopolysaccharide
→ these testing is not imp. in Opthalmic.

★ ISOTONIC SOLUTION

When Osmotic pressure of sol^n is equal to 0.9% NaCl or 1.9% Boric acid.

EVALUATION OF PARENTERAL PRODUCTS

LEAKER TEST (Packaging integrity test) – Only for ampoules, 1% Methylene blue dye & vaccum used.

CLARITY TEST (particulate matter test) – Instrument like – Light scattering (Nephelometer)
– Light absorption
– Electrical resistance (coulter counter).

PYROGEN TEST – Fever response in rabbits
Limulus test (lal test) – 5 to 10 times more sensitive than rabbit test.
Based on gelling of pyrogenic prep^n.

STERILITY TEST – Method ⇒ Membrane filteration.
⇒ Direct inoculation.
Incubation – for 2 weeks at 20 to 30 °C

PARENTERALS

NOTE :—

* Positive pressure is normally found in Aseptic & Sterile area (class 100 area)
* Aseptic process validation – sterile media fill "broth fills"
* Solid content of parenteral suspension usually range bet^{n}. 0.5 to 5% (Dextrose) may go to high as 30%

TABLET

✓ Important points to be remembered

(a)	In chewable tablet mannitol used as diluents. No disintegrating agent required.
(b)	Nitroglycerin & Isosorbide gives sublingually.
(c)	Diluents also known as fillers.
(d)	Lactose is mostly used Diluents.
(e)	5-80 % diluents can be used.

✓ Important diluents trade name

Diluents	Trade name
▷ Dextrose :-	Cerelose
▷ Sucrose :-	Sugartab, Dipac, Nutab.
▷ Microcrystalline cellulose	Avicel
▷ Starch :-	Emdex, Celutab, Sta Rx 1500
▷ Modified Starch :-	Primogel, Explotab.

✓ Note :-

- # Lactose gives maillard reaction with $-NH_2$ containing drug. Due to formation of furaldehyde
- # Mannitol has cooling effect due to negative heat of soln.
- # Sorbitol is optical isomer of mannitol.
- # Aspirin is directly compressed tablet so no need of diluents.
- # Saccharin 500 times sweeter than sugar but carcinogenic so currently Aspartame is used it is 200 times sweeter than sugar
- # Flavouring agents used 0.5 to 0.75% w/v

Excellent Lubricant	Excellent Antiadherant	Excellent Glidant
▷ Magnesium stearate ▷ Calcium Stearate	Talc, Corn starch	Colloidal Silica • Cab-o-sil • Aerosil • Syloid

Flow Properties	Angle of repose
Excellent	25-30
Good	31-35
Fair	36-40
Passable	41-45
Poor	46-55
Very Poor	56-65
Very very Poor	>66

Carr's Index	
Compressibility Index	
15%	→ Excellent
18%	→ Good
25%	→ Poor
100%	→ Very Poor

✓ Question asked from parts of Tablet machine :-

✓ Hopper	→ For holding & feeding.
✓ Dies	→ Define size & shape
✓ Punches	→ Compression of granules with die
✓ Camtrack	→ Guide Movement of Punches.
✓ Turrets	→ Hold upper & lower Punches.
✓ Feeding machine	→ Used for moving.
✓ Die table	→ Portion holding the dies.

Note :-

- ▷ Shape factor should be 6 for granule.
- ▷ Surface area is measured by
  - ✓ Gas adsorption method.
  - ✓ Air permeability method.
- Strength is determined by plaing of granules between anvils (Tumbler test).
- Slugging process is related to Dry granulation.

Comparision Box ↓

Variables	Disintegration	Dissolution
✓ Temperature	37 ± 2°C	37 ± 0.5 °C
✓ Speed	28-32 cps	50-100
✓ Distance below surface of liquid	2.5 cm (25mm)	2.3-2.7 cm (23-27 mm)

Dissolution Apparatus I (Basket), II (Paddle) → USP & BP
Reverse in IP

TABLET

* Mostly asked questions from Tablet defects / Coating defects

	Types	Defects
①	Mottling	Unequal distribution of colour
②	Orange peel effect	Inadequate spreading of coating material
③	Capping	Seperation of top or bottom due to air entrapment
④	Lamination	Separation of tablet into two or more layers
⑤	Sticking	Adhesion of granulation material to the die wall
⑥	Picking	Adhesion to the face of punch
⑦	Cracking	when internal stress exceeds tensile strength of film.

* Important points in Tablet coating

- Coating is done by four types Sugar, film, Enteric & spaialized coating.
- Alcoholic soln is used for Sealing [Alcoholic soln of zein & shellac].
- Polishing is done by Bees wax, Paraffin & Carnuba wax mostly.
- Fluidized bed prcess also known as Air suspension coating.

* Mostly asked examples in questions:-

Diluents :-	Lactose, Dextrose, Mannitol, Sorbitol, Avicel, Dicalcium phosphate.
Granulating Agent	water, starch, mucilage, tragacanth mucilage, alcohol acetone
Binder & adhesive	Starch, sucrose, Gelatin, Cellulose derivative, Cross linked PVP.
Lubricants :-	Magnesium & calcium stearate.
Antiadherants :-	Talc, Corn starch etc.
Colidants :-	Colloidal silica, Corn starch
Disintegrants :-	Alginate, PVP, Primogel, SLS. Veagum (Magnisium aluminium silicate)
Superdisintegrants :-	Sodium Starch glycolate, Crosspovidone, Croscarmelose.
Sweetning Agents :-	Mannitol, Aspartame, Sacharine.
Subcoating binders	Gelatin, Sugarcane, PEG
Subcoating Dusting Powder	TiO_2, Talc, $CaCO_3$
Polishing Agent :-	Bees wax, Paraffin, Carnauba wax.
film Coating materials :-	HPMC, MHEC, PVP, PEG, Acrylated Polymer, (Eudragit E)
Enteric Coating materials :-	phthalate derivatives, Eudragit (L,S)
Plasticizers :-	Tween, Span, Castor oil, PEG, Glycerin
Colorants :-	Iron oxide pigment (Red colour), Titanium Dioxide (white), Lakes, Caramel, Caretonoids etc.

TABLET

Evaluation of Tablets :-

Evaluation Test	Test Parameters	Determined By	Standard values & others points to be remembered
① General Appearance	✓ Size & Shape ▸ Compressed tablets shape & dimentions	By tooling during the compression Process	± 5 %
	▸ Crown thickness of tablet	By micrometer	
	▸ Total crown thickness	By vernier calliper	
	✓ Colour	By • Reflectance spectrophotometer • Tristimulus - Colorimetry • Micro-reflectance photometry	Colour uniformaty testing
② Tablet Hardness	✓ Hardness / strength / diametric compression test	By ✓ Monsetto tester ✓ Strong cobb tester ✓ Pfizer & Erweka tester	minimum 4kg
③ Friability	✓ Drug loss during transportation. Note Tablet falls- 6 inch Speed - 25 rpm Time - 4 min. Total revolution - 100	By Roche friabilator	Not more than 1 % (I.P) % friability = $\frac{\text{Initial wt} - \text{final wt}}{\text{Initial wt}} \times 100$ # 0.5-1 % (USP)
④ Weight Variation	Randomly 20 select → if 18 tablets remain 90mg to 110mg If 2 tablets remains within 80 to 120 mg		Passed batch
	# Average wt. of Tablets		
	IP: 80 mg / less	USP: 130 mg or less	± 10 %
	80 - 250 mg	130 - 324 mg	± 7.5 %
	More than 250mg	More than 324	± 5 %
⑤ Uniformity of content	30 taken → 1st 10 analysed if 9 → 85-115 % & 10 → 75-125 % Other 20 is not 85-115 % range outside	By Analytical Technique	Passed Batch

SOLUTION

- Aromatic water → Volatile material in H_2O
- Syrup → Contain 85% w/v Sucrose or 66.7% w/w Sucrose
- Elixir → Sweetened hydroalcoholic soln
- Spirits → Alcoholic or hydroalcoholic soln.
- Linctuses → relief of cough
- Liniment → Alcoholic & oil liquid, rubbing on to the affected area
- Lotions → Aqueous, alcoholic & oily liquid, without rubbing on the affected area

Solubility as per IP

- Very soluble → less than 1
- Freely soluble → 1-10
- Soluble → 10-30
- Sparingly soluble → 30-100
- Slightly soluble → 100-1000
- very slightly soluble → 1000-10,000
- Insoluble → More than 10,000
- Solubility study can be determined at 30°C
- Henry's law → Measure the solubility of gases in solvents

* Sweetening agent ⇒ 1) Saccharine (Approx 250-500 times as sweet as sugar)

2) Aspartame (Approx 200 times than sucrose)

⇒ Aspartame is methyl ester of Aspartic acid + phenylalanine

* 5-10% ethanol used in formulat^n. for antimicrobial agent

* Monosodium gluconate glutamate has been widely used in food industry to mask the metallic taste.

* Taste property improves by sodium bicarbonate, Gluconate, lactose

SUPPOSITORIES

- Solid dosage form
- Insertion into body cavity rectum, vagina, urethra

Types of suppositories :-

- Rectal suppositories
- Vaginal suppositories (Pessaries)
- Urethral suppositories (Bougies)
- Nasal suppositories
- Ear cones

Ideal Suppository base :-

- Melt at body temperature
- Inert, non irritating & non sensitizing
- If the base is fatty than
  - Acid value - Below 0.2
  - Saponification value - 200 to 245
  - Iodine value - Less than 7

Suppository base :-

Suppository base	Example
Oleaginous (fatty) base	Cocoa butter (Theobroma oil), Synthetic fats Hydrogenated palm kernel oil
Aqueous Base	Glycerinated gelatin (14% Gelatin + 70% glycerine + H_2O)
Emulsifying Base	Massa estarinum, Witepsol, Massupol

Cocoa butter

- Most widely used suppository base
- Melting point = 30-35°C
- Iodine value = 34-38
- Acid value not higher than 4
- Polymorphism - α, β, β' & γ
- Melting point of γ = 24°C
- Melting point of β' = 28-31°C
- Melting point of β = 34-35°C
- Melting point of γ = 18°C
- β form is more stable

Factors affecting drug absorption from rectal suppositories :-

- Physiological factor - pH of rectal mucosa.
- Physiochemical characteristic of drug -
  - Particle size more - ↓se absorption
  - Presence of surfactant - ↑se (NaI)
    ↓se (Phenol)
- physicochemical characteristic of the base & adjuvant
  - Melting point of base
  - cross linking $\propto \frac{1}{\text{Release of drug}}$
  - Viscosity $\propto \frac{1}{\text{Release of drug}}$.

SUPPOSITORIES

Stability problems in suppositories :-

- **Water**
  - present accelerate oxidation of fats.
  - Evaporate cause crystallization
- **Incompatibility**
  - Silver salt, Tannic acid, Aminopyrine, sulphonamide incompatible with PEG base
  - penicillin → stable in cocoa butter
    → unstable in PEG
- **Viscosity :-**
  - If less - Non-uniform storage problem
  - for ↑ the viscosity 2% monosterate
- **Blooming**
  - White powder deposited at surface
- **Brittleness**
- **Rancidity & Antioxidant**
  - Calculated by peroxide value
  - Example of antioxidant
    - α, β tocopheral (vit E)
    - Grossypol
    - Sesamol
    - Propyl gallate

⇒ Polyoxyethylene sorbitan fatty acid esters (Tween) & polyoxyethylene stearates (Myrj) are example of water dispersible suppository base

⇒ The tensile of suppository is measured by - Breaking strength.

⇒ PEG base is used in the preparation of vaginal suppositories.

⇒ Cetyl alcohol is used as coating material in the preparation of coated suppositories.

⇒ Silver nitrate - increase the melting point of cocoa butter.

⇒ Triglycerides of saturated vegetable oil is the chemical nature of witepsol used as a suppository base.

AEROSOLS

* TYPES OF AEROSOLS

1) Two phase (gas & liquid)
2) Three phase (gas, liquid & solid or liquid

* Classification of Aerosols

1) Metered dose inhaler
2) Powdered drug
3) Nebulizer
4) Dental spray
5) Skin spray

* classification of Propellant

For oral & Inhalational	Topical
Fluorinated Hydrocarbons →	Hydrocarbons → propane, Butane, Isobutane
• Trichloromonofluromethane (011)	Compressed gases → Nitrous oxide, Nitrogen, CO_2
• Dichlorodifluromethane (012)	
• Dichlorotetrafluroethane (0114)	

* HYDROCHLOROFLUOROCARBONS & HYDROFLUROCARBONS (# low ozone depleting)

- → Chlorodifluoromethane ($CHClF_2$, P_{22})
- → Trifluro monofluoro ethane (CH_3CH_2F, P_{134a})
- → Chlorodifluoroethane (CH_3CClF_2, P_{142b})
- → Difluoroethane (CH_3CHF_2, P_{152a})
- → Heptafluoropropane (CF_3CHFCF_3, P_{227})

* NAMING OF CFC

⇒ 1st digit represents - [nC-1]
⇒ 2nd digit represents - [nH+1]
⇒ 3rd digit represents - [nF]

* CALCULATION

Dalton's law :-

$$P = P_1 + P_2 + P_3$$

Raoult's law :-

$$P = (x \times P_0')$$

AEROSOLS

* COMPONENTS OF VALVE

→ Ferrule or mouth cap ⇒ Al, Brass
→ Valve body or housing ⇒ Nylon, Al (opening 0.0132 - 0.08 inch)
→ Stem ⇒ Nylon, Al
→ Gasket ⇒ Buna-N & Neoprene
→ Spring ⇒ Stainless steel
→ Dip tube ⇒ Polypropylene & polyethylene

* EVALUATION OF AEROSOL

1. Flame Projection
   → extension of an open flame
   → product is spray 4 sec. into a Flame
   → Measured by ruler
   → Determine flammability & combustibility
2. Flash point
   → Tag open cup apparatus
   → Temp - 25°c
3. Vapour pressure → pressure gauge
4. Density → Hydrometer & pycnometer
5. Moisture content → Karl-Fisher method & Gas chromatography
6. Identification of Propellants → Gas chromatography
   IR Spectroscopy
7. Foam stability
   → visual evaluation
   → Rotational viscometer
8. Particle size
   → Cascade impactor (0.1 - 30um)
   → light scatter decay

SUSPENSION

- Thermodynamic stable, heterogenous system
- Size of the particle → 0.5 - 5 μm
- Prolonged action → ⇒ Protamine zinc - Insulin suspension
  ⇒ Procaine penicillin G suspension
- Dilute suspension → 2-10 w/v solid
- Concentrated suspension → 50% w/v solid

Flocculated Suspension	Deflocculated Suspension
Particles form loose aggregate and form network like structure.	Particle exists as separate entities.
Rate of sedimentation is high	Rate of sedimentation is low.
Sediment is easy to redisperse	Sediment is difficult to redisperse
Sediment is loosly packed & not form a hard cake	Sediment is very closely packed & form a hard cake

* For an ideal suspension, the sedimentation volume should be ⟶ equal to one

* Preparation of structured vehicle → Methyl cellulose is used

* colloidal material is used common in the prep^{n} of structured vehicle ⟶ Hydrophilic

* Structured vehicle is included in the formulation Suspension, in order to → Prevent the sedimentation of particle

* In the extemporaneous prep^{n} of Suspension levigation is used to ⟶ Reduced particle size

* DLVO Theory is → Used to explain stability ointments
Used to explain Brownian movements of colloids

* The amount of vehicle needed to produce pourability is denoted by → Flow point

SUSPENSION

★ Formulation of Suspension

Flocculating agents	Suspending agent, Thickning agent	Protective colloids	Wetting agent	Preservative	Organo-leptic additives
Eg:- SLS, Tweens, span, carbowax	Eg:- • Inorganic agent → clay, $Al(OH)_3$ • Synthetic → carbomer, Colloidal SiO_2 • polysaccharide → Acacia, starch, Talc, MC, HPMC	Eg:- Gelatin, Natural gum, cellulose derivatives	Eg:- → Alcohol in tragacanth mucilage → Gelatin in sodium alginate	Eg:- Benzoic ā Methyl paraben Sodium benzoate	→ Sweetning agent → Colouring agent → Flavouring agent

* Zeta potential of suspension is helpful to find out the → Stability of suspension
* Stoke's law ⇒ Rate of Sedimentation is expressed

$$\frac{dc}{dt} = \frac{D^2(d_1 - d_2)g}{18\eta}$$

* Sedimentation volume = 1 (No sedimentation)
  Sedimentation volume = 0 (Complete sedimentation)
* Stokes law applicable to deflocculated system — where particle settle independently

* Deflocculated suspension shows ⟶ Newtonian flow
* Flocculated suspension shows ⟶ Non-Newtonian Flow
* The protamine – zinc suspension is prepared by a method viz. → Altered pH precipitation
* Which of the wetting agent used in parenteral suspensions ⟶ SLS
* Carboxy vinyl polymer is a ⟶ Carbomer

SUSPENSION

* **Zeta potential →**
  1) The measurement of zeta potential gives → •) Charge on particles, •) Stability of suspension
  2) Calcium hydrogen phosphate is dissolved in H_2O. The apparent zeta potential initially is → Negative
  3) The determination of change in the particle size of suspension is used → Zeta meter

* **Dilute** → 0.5 to 2% solid – stokes law apply
* **Concentration** → 5 to 10% solid – Hinderance occurs

CAPSULE

# Not Used for Administering –	# Used to –
• extremely soluble material (KCl, KBr, NH_4Cl, I) cause → Irritation • Higly efflorescent cause → softness of shell • Higly Deliquescent cause → brittleness of shell	→ Mask the taste → Mask the odour.

GELATIN :– Heterogeneous product, derived by Hydrolytic extraction of animal collagen.

TYPES OF GELATIN

TYPE	SOURCE	PROCESSING	ISO-ELECTRIC POINT
Type-A	Pork skin	Acid Processed	PH – 9
Type-B	Bones	Alkali Processed	PH – 4.7

* HARD GELATIN CAPSULE (HGC) :–

Components of HGC Shell

- Capsule shell – Gelatin
- Dyes – Indigo, erythrosine.
- Opacities – TiO_2
- Plasticizer – sorbitol, Glycerine
- Preservative – Methyl paraben & Propyl paraben (4:1)

size & filling Capacity of gelatin

Capsule size	Size (in mm)	Vol. (ml)	Wt. (mg)
000	26.3	1.37	950
00	23.7	0.95	650
0	21.8	0.75	450
1	19.2	0.55	300
2	18.3	0.40	250
3	15.3	0.30	200
4	14.7	0.25	150
5	11.9	0.15	100

Method of Manufacturing of empty HGC shell.

- Centrifugal casting method
- Dip pin method (mostly used) (Thickness depend on speed & time

STEPS	DESCRIPTION
⇒ Dipping	Temp. of pin = 22°C, Sol^n temp = 50°C Time of Dipping = 12 sec.
⇒ Spinning	Pins are rotated.
⇒ Drying	By use of Dry air & Dehumidification.
⇒ Stripping	By Bronze jaws.
⇒ Trimming	By stationary knives.
⇒ Joining	Cap & Body are joined.
⇒ Polishing	By Polymer.

CAPSULE

Process of filled HGC :-

* Preparing the formulation.
* Selection of the size of capsule
* Proper mixing & Blending.
* filling the capsule shells.
* Capsule sealing & shorting.
* Cleaning & polishing.

Method of Cleaning & Polishing

* Pan Polishing - Accele cota tablet, coating pan used.
* Cloth dusting.
* Brushing
* Erweka KEA Machine.
* Scidenader PM 60 Machine.

Capsule filling Machine

- Hofliger & Karg → Bulk powder
- Perry → Bulk powder
- Farmatic → Bulk powder.
- Macofar → Bulk powder.
- Eli Lilly → Pellet, granules
- Zanasi → Powder, pellet, granules
- Osaka → Based on vibration prin.
- MG_2 → Continuous filling of powder.
- Rotofill → Pellets.

Capsule Weighing Machine

- Vericap - 1200
- Rotoweigh.

Condition for Capsule

Storage = 100°F (35°C)
Area temp. = 22°C (Processing)
Humidity = 30 - 45 %
Moisture Content = 12 - 16
Gelatin : Plasticizer = 1 : 0.4

SOFT GELATIN CAPSULE :-

Components are :-

- Gelatin - Bloom strength = 150 - 120, Viscosity = 25-45 millipoise
  Iron content = NMT 15 PPM
- Plasticizers - Sorbitol, glycerin, PEG. [Gelatin : Plasticizer = 1 : 0.8]
- Preservatives - 0.2 % Methyl paraben : Propyl paraben = 4 : 1
- Opacifiers - TiO_2
- Fumaric acid - 1 % ↑ acid solubility & ↓ aldehyde tanning.
- Sugar - 5 %
- Essential oil - 2 %
- Formalin - Retards dissolution of gelatin.
- Coating material - Salol, CAP, shellac.
- SO_2 - 0.15 % of gelatin (Prevent Decomposition.

CAPSULE

Evaluation of Capsule :-

(1.) Invariability Test

Weight Variation

Avg. wt. of caps.	% deviation
less than 300 mg	10 %
300 mg or more	7.5 %

Content Uniformity

test pass if, all 30 capsule are within 75 - 125 % range & NLT 27 of 30 are within 85 - 115 % range.

(2.) Dissolution test - Rotating Basket type.

(3.) Disintegration test :

- For HGC = 30 min.
- For SGC = 60 min.

(4.) Stability test :-

⇒ Shell integrity test.

⇒ Determination of self life.

Note :-

★ Soft spot (Blooming) - Site at which capsule lie next to the tray or against another capsule.

★ Bloating - At high humidity (60 %) capsule size increases.

★ Foreign capsule - Unfilled capsule.

STERILIZATION

process designated to produce a sterile state.

* Some basic terms used :-

1) Sterility : condition of freedom from living organisms. (absolute)
2) D-value (Decimal Reduction Time) :- Time or dose required for microbial population to decline by one decimal point.
3) Z-value (Thermal destruction value) :- degree of temperature required for 1 log reduction in D value.
4) F-value : time in minutes at a specific temp. (usually 250°F / 121°C) needed to kill a population of cells or spores.
5) Holding Time : Time required for killing the organism
6) Thermal Death Time : (TDT) : shortest time needed to kill all organisms in a microbial suspension.

Sterilization Methods :

(A). Sterilization by HEAT :

1. Dry heat Sterilization :

used for : oils, petroleum jellies, talcum powder, glass & metallic apparatus.

* Microorganisms more resistant to dry heat than moist heat.

@ Flaming :

used for : forceps, needles, scalpels, metal spatulas etc.

Bunsen flame to the surface for 5 seconds.

ⓑ Hot air oven :

180 minutes at 180°C
or 45 minutes at 260°C.

MoA : Destruction by means of heat & it is an Oxidation Process.

For glasswares & oily sol^{n} : 160C for 1 hour.

2. Moist heat Sterilization :

MoA : Coagulation of proteins in the cell.

Used for : porous materials such as cotton wool, stoppers, paper, cloth wrappers, bundles of surgical linen etc.

Temp °C	Pressure	Holding time (in min.)
115-116	10	30
121-123	15	15
126-129	20	10
134-138	32	3

STERILIZATION

(3) Tyndallization :

→ Also known as 'fractional Sterilization'
→ devised by JOHN Tyndall
→ 80°C for 1 hour or at 100°C for less time on 3 successive days.
→ Kills dormant, resistant spores also
→ No special apparatus required.

(4) Heating with a bactericide :

→ Bactericide are more effective at high temp than low temp.
→ offical in B.P. & consists of heating at 90-100°C for 30 minutes.

For injections :

Chlorocresol	0.2% w/v
Phenylmercuric acetate	0.002% w/v
Benzalkonium chloride	0.01% w/v
Thiomersal	0.01% w/v

(5) Pasteurization :

→ devised by Pasteur.
→ It only reduces the viable count by 97 to 99%. but does not kill spores.
→ applied to milk in dairies.

(6) Dry heat above 150° C.

bacterial spores passing through an extremely heated furnace can be sterilized in 0.4-0.6 sec. at 225°C

* Note :

More uses of UV radiation

i) inactivate viruses & bacteria in vaccine production.
ii) also used for irradiation of incoming and/or internal air of the sterile filling areas of antibiotic.
iii) prevent cross infection of hospitals & schools etc.

[B.] Sterilization by Radiation :

→ Also known as 'Cold sterilization'.

MoA → interference in the metabolism of the cell.

(1). Ultraviolet light :

→ 2537 A° possess greatest activity in destroying m.o.
→ reduction of air borne contamination & maintenance of aseptic areas & rooms.

MoA : UV light absorbed by nucleic acids of the cell wall where it does the greatest damage.

Uses : to destroy the viruses of homologous serum jaundice in blood.

(2). Ionizing Radiation :

Produced
- directly → from charged particles
- Indirectly → " gamma rays

→ Have highest penetrating powers.

MoA → destroy microbes by stopping reproduction as a result of lethal mutations.

Uses : i) preservation of foods.
ii) injection products of antibiotics like benzylpenicillin, streptomycin sulphate

STERILIZATION

* Note:

UNIT for measurement of radiation doses:

1) Roentgen (r) → fundamental unit for radiation doeses.
   ↳ is defined in terms of the number of ionizations produced per unit vol. of air.

2) rad. → Another unit which represents an energy absorption of 100 ergs per gram of material.

[C]. Sterilization by Filtration:

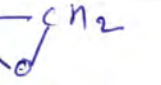
→ Used for sterilization of heat-labile solutions.
→ * Official in I.P. for sterilization of certain injection soln.

Efficient filters: should be able to retain Serratia marcescens.
Av. pore diameter = 0.75 µm or less.

Commonly used filters are:
→ porcelain filters, diatomaceous earth filters, ~~ab~~ asbestos pad filters, sintered glass filters, membrane filters & Ultrafilters.

MoA: removal of microbes (Physical) from sample

[D]. Chemical Processes of Sterilization (Gaseous Sterilization)

① Ethylene Oxide: 

→ Simplest cyclic ether
→ highly inflammable
→ may be explosive at conc > 3% in air.
→ made safe by mixing with inert gases CO_2 etc.

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② Ozone:

→ Pleasant smelling but irritant & toxic gas

MOA → general protoplasmic oxidant

Uses:

i) disinfection of water

ii) preservation of foods from spoilage during bulk storage

③ Formaldehyde:

Used for: fumigation of rooms & hospital blankets.

→ Irritant & pungent

→ kills all bacteria, including pores, rapidly.

→ Inactivated by proteins & organic matter.

④ β-Propiolactone (BPL):

→ highly bactericidal

→ conc used - 5 mg/litre or less.

Uses:

i) decontaminating rooms, chamber & buildings.

ii) highly virucidal but carcinogenic to animals.