Liquid Orals

By
Mr. R.M.Kuwar
(Department of Pharmaceutics)
JES's College of Pharmacy, Nandurbar

CONTENTS:-

- Definition of liquid orals
- Types of liquid orals
- Suspensions
- Emulsion
- Solutions

DEFINITION:-

Liquid orals are the homogeneous liquid preparations containing one or more active ingredients with or without additives dissolved in a suitable vehicle,meant for oral administration.

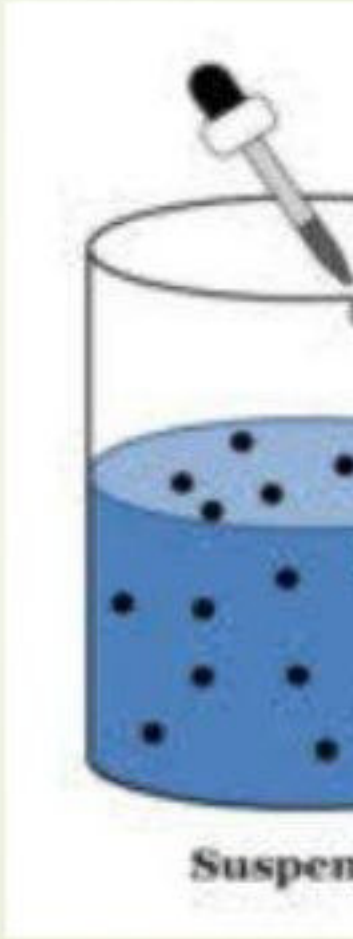
TYPES OF LIQUID ORALS:-

- SUSPENSIONS
- EMULSIONS
- SOLUTIONS

SUSPENSIONS

DEFINITION:-

Suspensions are the biphasic liquid osage form of medicament in which the nely divided solid particles are suspended r dispersed in a liquid or semisolid vehicle ith the help of suspending agent.The solid article is the 'dispersed phase' or iscontinuous phase' whereas the liquid ehicle is the 'continuous phase'.



ADVANTAGES:-

- Can improve chemical stability of certain drugs.
- Higher rate of bioavailability,as order of bioavailability is:-

Solution>Suspension>Capsules>Compressed tablets

DISADVANTAGES:-

- Physical stability,sedimentation and compaction
- Bulky,handling require care.
- Uniform drug delivery cannot be achieved sometimes.

IDEAL PROPERTIES OF SUSPENSIONS

1. The dispersed particles should not settle readily and the settled particles should redisperse immediately on shakin
2. The particles shouldn't form a cake on settling.
3. The viscosity should be such that the preparation can be easily poured.
4. It should be chemically stable.
5. Suspensions for internal use must be palatable and suspension for external use must be free from gritty part

TYPES OF SUSPENSIONS:-

Depending upon particle nature/disperse particle nature the suspensions are of two types:-

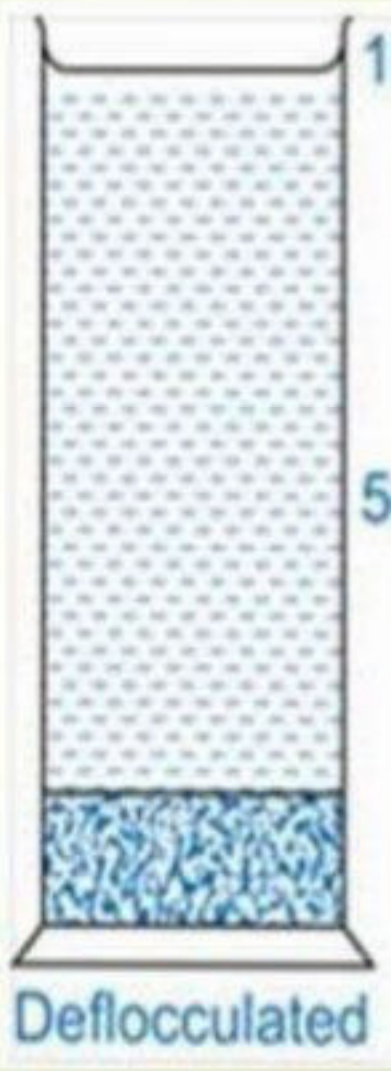
1. Flocculated suspensions
2. Non-flocculated/deflocculated suspensions.

FLOCCULATED SUSPENSIONS:-

Suspension in which particles are weakly bonded,settle rapidly,donot form a cake and are easily resuspended with a minimum of agitation.

DEFLOCCULATED SUSPENSIONS:-

Suspension in which particles settle slowly and eventually form a sediment in which aggregation occurs with the resultant formation of a hard cake which is difficult to resuspend.



Differences between flocculated an deflocculated suspension

Flocculated	Non-flocculated
articles forms loose ggregates and form a etwork like structure	1. Particles exist as separate en
ate of sedimentation is high	2. Rate of sedimentation is slo
ediment is rapidly formed	3. Sediment is slowly formed
ediment is loosely packed nd doesn't form a hard cake	4. Sediment is very closely pa and a hard cake is formed
ediment is easy to redisperse	5. Sediment is difficult to redi
uspension is not pleasing in ppearance	6. Suspension is pleasing in appearance
he floccules stick to the ides of the bottle	7. They don't stick to the sides bottle

FORMULATION OF SUSPENSIONS:-

1. Flocculating agents.
2. Suspending agents/thickening agents.
3. Wetting agents.
4. Dispersing agents.
5. Preservatives.
6. Organoleptic additives.

PREPARATION OF SUSPENSION

Step 1:

uspensions are prepared by grinding the insoluble materials in the mortar To a smooth paste
vehicle containing the wetting agent.

Step 2:

soluble ingredients are dissolved in same portion of the vehicle and added to the smooth paste
to get slurry.

Step 3:

he slurry is transformed to a graduated cylinder, the mortar is rinsed with successive portion
vehicle.

Step 4:Decide whether the solids are

- Suspended in a structured vehicle
- Flocculated
- Flocculated and then suspended

Add the vehicle containing the suspending agent (or) flocculating agent

tep-5:

Make up the dispersion to the final volume .

Thus suspension is prepared.

STABILITY OF SUSPENSIONS:-

A stable suspension can be redispersed homogenously throughout its shelf life.The more stable pharmaceutical suspensions are flocculated i.e.,the suspended particles are bonded together physically to form a loose cake.

EVALUATION OF SUSPENSION STABILITY:-

The following are commonly used for evaluat the physical stability of suspensions:-

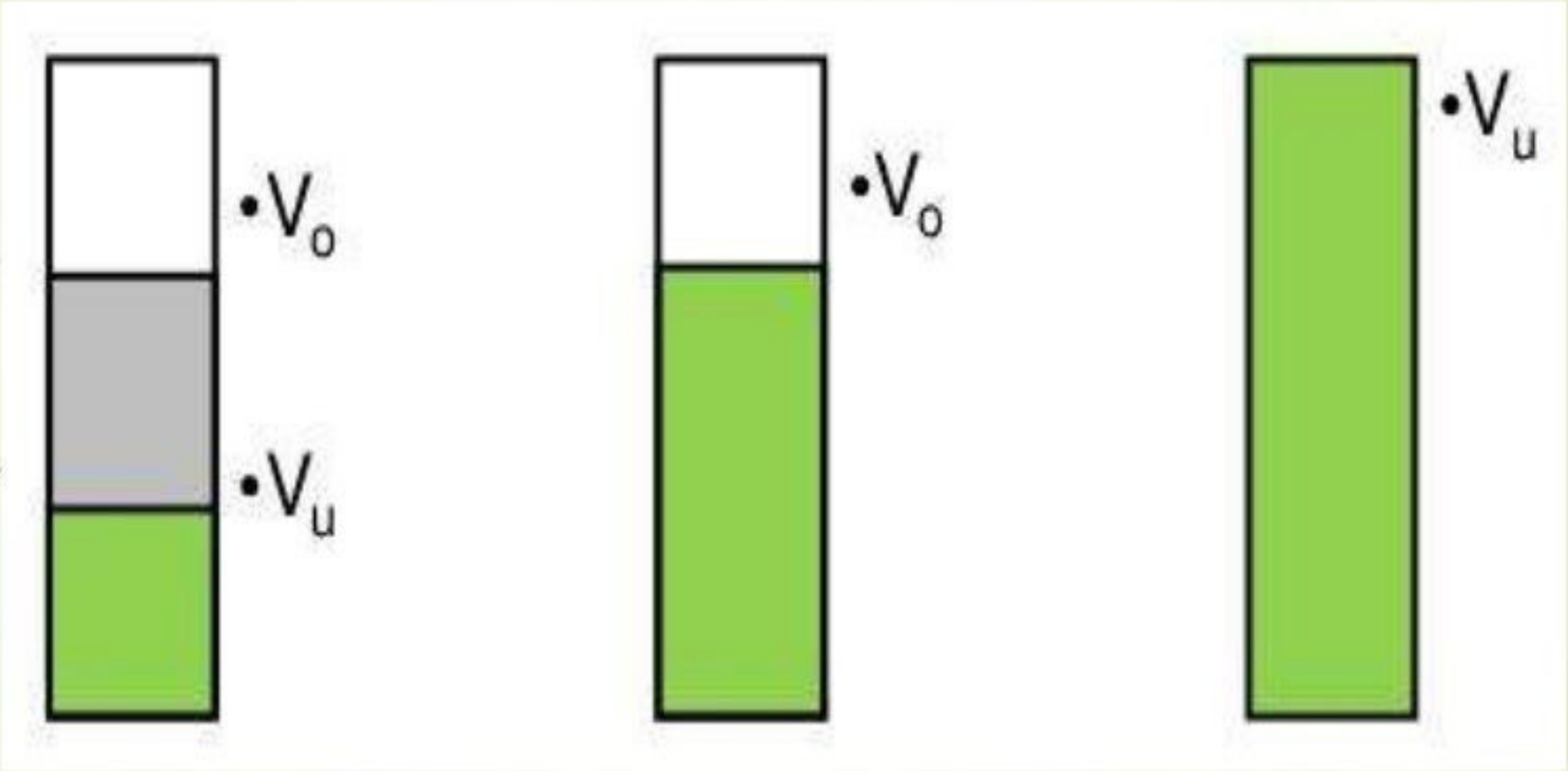
1. Sedimentation method.
2. Rheological method.
3. Electrokinetic method.
4. Micromeritic method.

1.SEDIMENTATION METHOD:-

It is determined by keeping a measured volum suspension in a graduated cylinder in an undisturb position for a definite period of time,the ultimate volume (V_0) and the intial volume (V_u) of the sedim is to be noted.

Sedimentation volume is a ratio of the ultimat volume of sediment (V_0) to the original volume of t sediment (V_U) before settling.

Sedimentation volume $F=V_0/V_U$



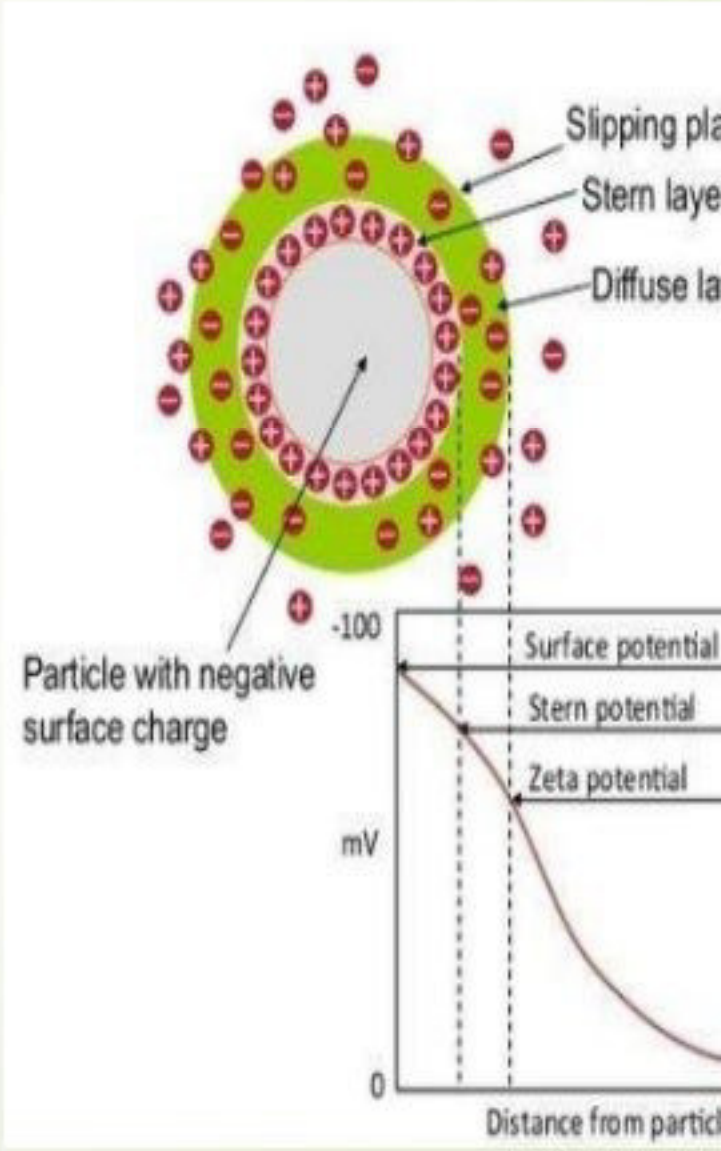
Sedimentation rate of a suspension

2.RHEOLOGICAL METHOD:-

- It provides information about settling behaviour.
- The arrangement of the vehicle and the particle structural features.
- Brookfield viscometer is used to study the viscosity of the suspension.If viscosity of the suspension increases,the stability of the suspension increases.

3.ELECTROKINETIC METHOD:-

The determination of surface electric charge or zeta potential is helpful to find out the stability of suspension.Zeta potential can be calculated from the migration of particle measured by the electrophoretic method.



4.MICROMERITIC METHOD:-

The stability of suspension depends on the particle size of the disperse phase.The size of the particle in a suspension may grow and ultimately leads to the formation of clumps or caking.So,any change in particle size distribution with reference to time gives a stable suspension.The particle size can be studied by microscopy or coulter-countered method.

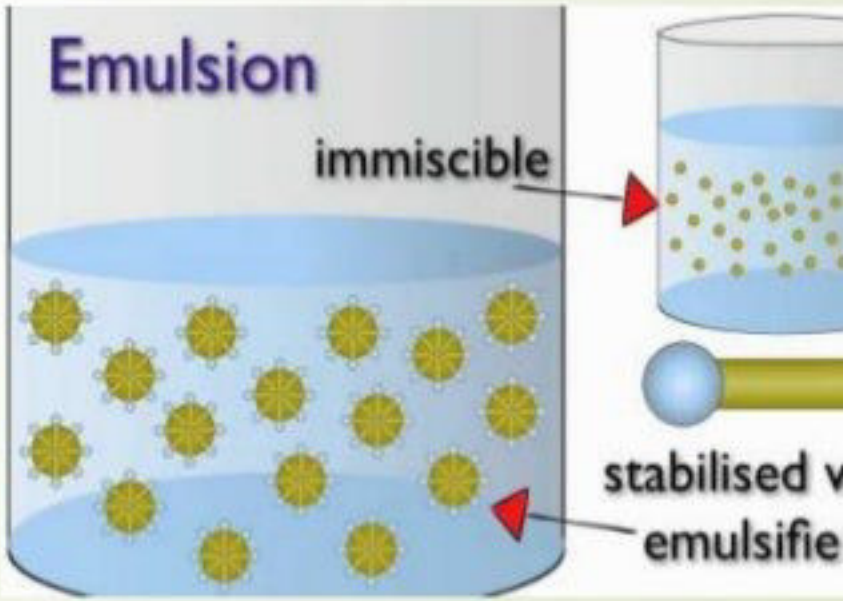
EMULSIONS

Cream: Oil-in-Water

Butter: Water-in-Oil

DEFINITION:-

An emulsion is defined as a dibasic or heterogenous liquid preparation immiscible liquids which is dispersed as a minute globules in another liquid by adding emulsifying agent.



CLASSIFICATION OF EMULSIONS:-

Emulsions can be classified into the following types:-

1. Oil in water (o/w) type of emulsion.
2. Water in oil (w/o) type of emulsion.
3. Microemulsions
4. Multiple/double emulsion.

ADVANTAGES:-

- Mask the unpleasant taste.
- Sustained release medication.
- Inert and chemically non-reactive.
- Reasonably odourless & cost effective.

DISADVANTAGES:-

- Packing,handling & storage is difficult.
- Thermodynamically unstable & have short she life.
- Leads to creaming & cracking.
- Leads to phase inversion.

FORMULATION OF EMULSIONS:-

1. Selection of phases.
2. Phase volume ratio.
3. Choice of emulgent.
4. Antimicrobial agents.
5. Anti-oxidants.
6. Viscosifiers/consistency agents.
7. Colouring agents.
8. Sweetening agents.
9. Flavouring agents.
10. Emulsifying agents.

IDENTIFICATION TESTS:-

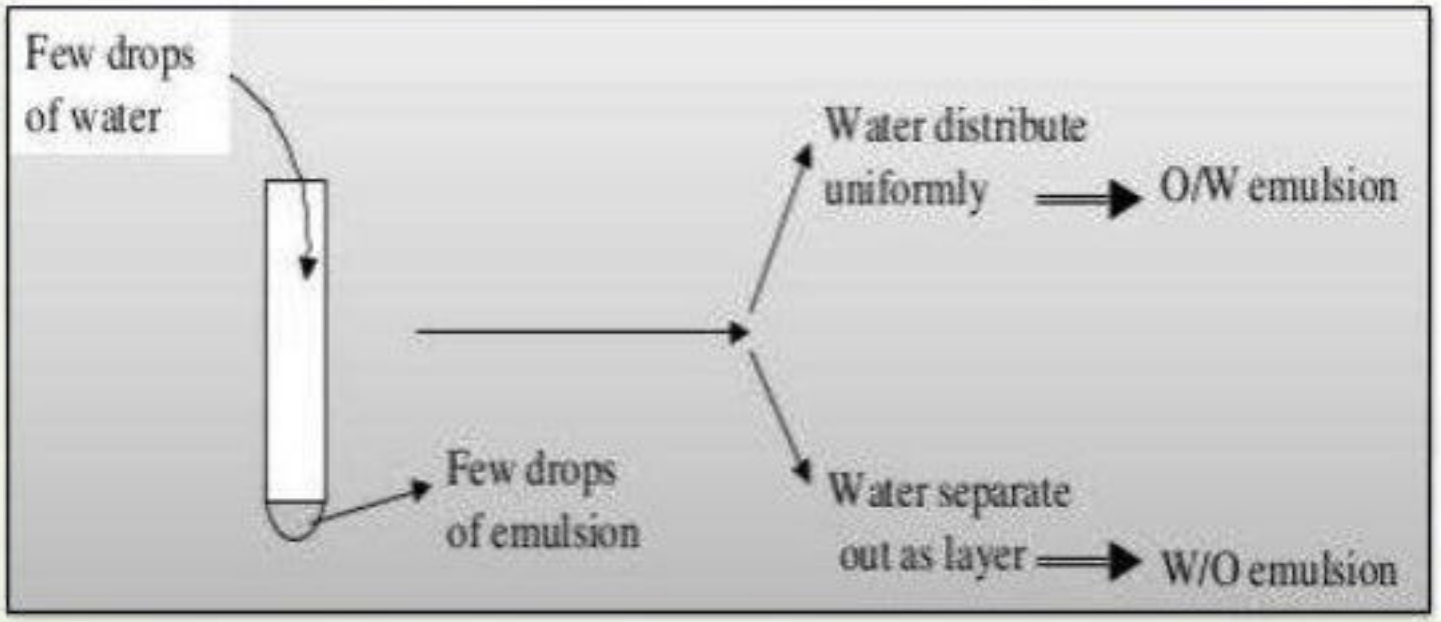
The type of emulsion can be determined by the following tests:-

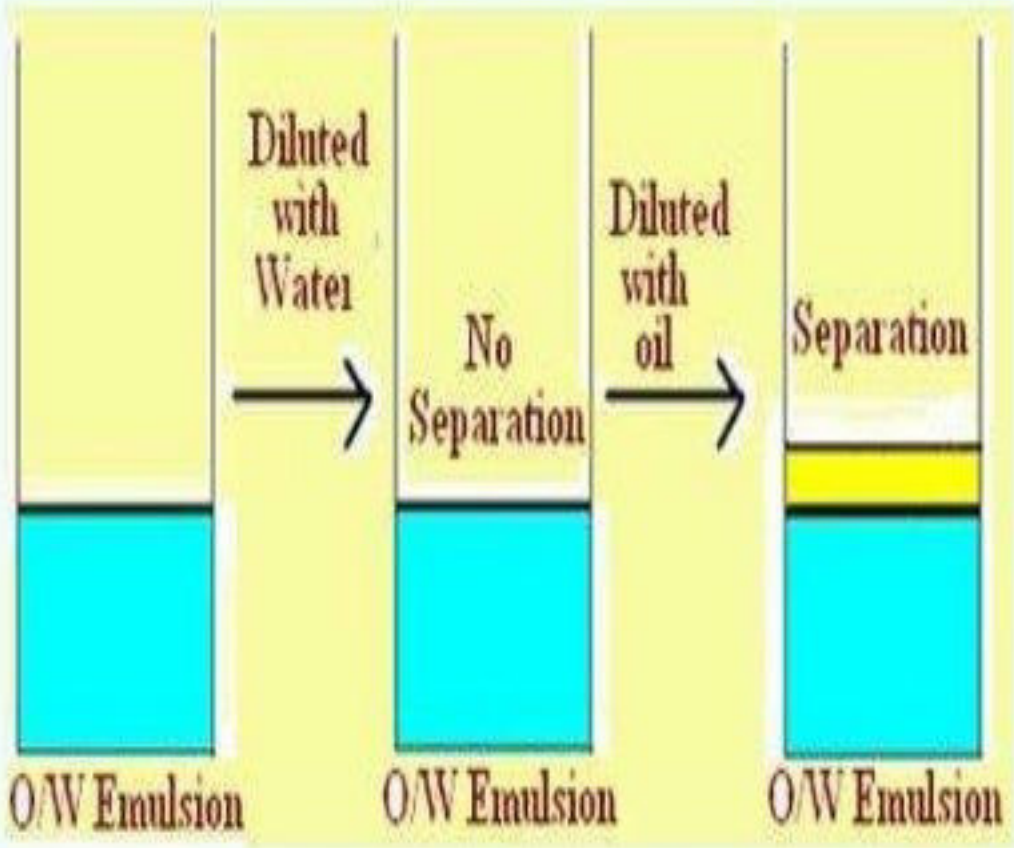
1. Dilution test.
2. Conductivity test.
3. Dye test.
4. Fluorescence test.
5. Cobalt chloride test ($CoCl_2$).

1.DILUTION TEST:-

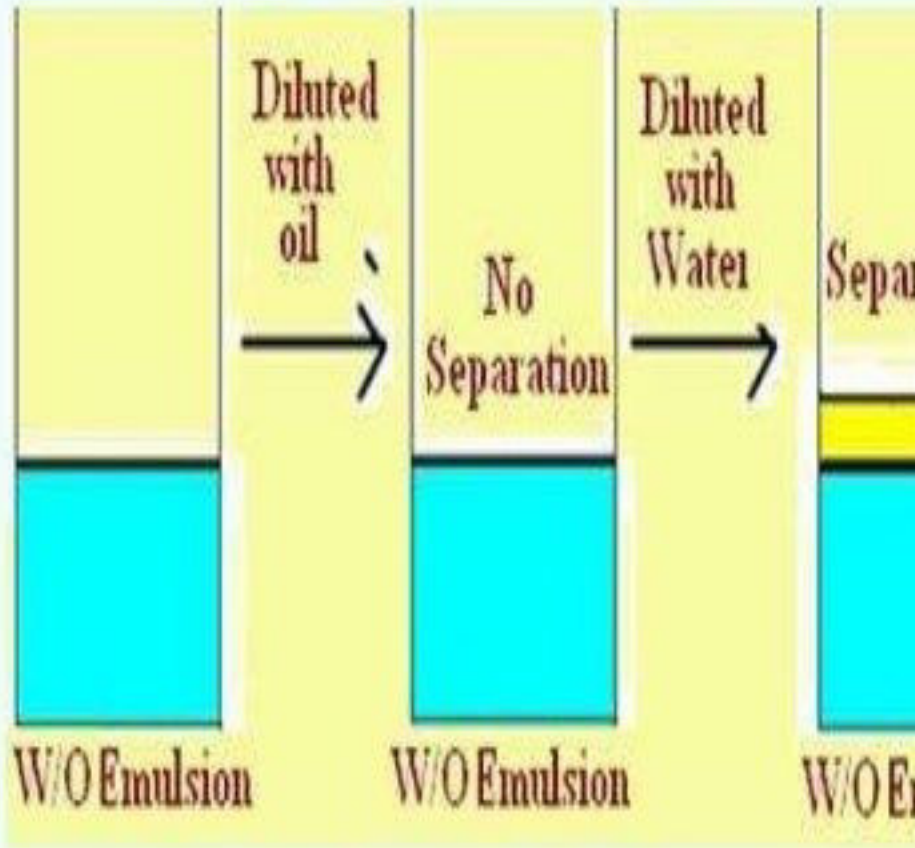
This test is based on the solubility of externa phase of emulsion.

- o/w emulsion can be diluted with water.
- w/o emulsion can be diluted with oil.





Dilution Test for oil in water emulsion

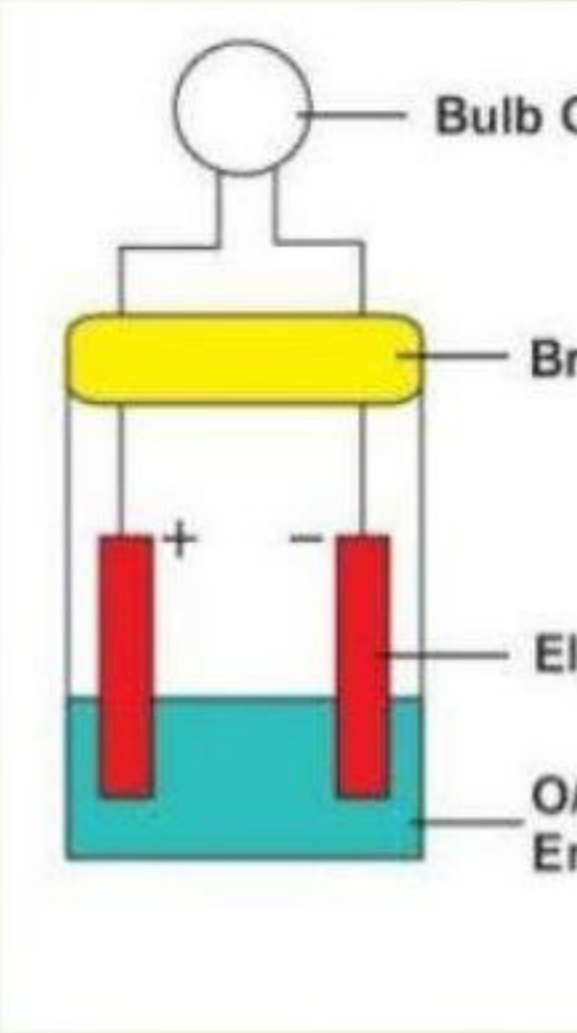


Dilution test for water in oil emul

2.CONDUCTIVITY TEST:-

The basic principle of this test is that water is a good conductor of electricity. Therefore in case of o/w emulsion this test will be +ve as water is the external phase.

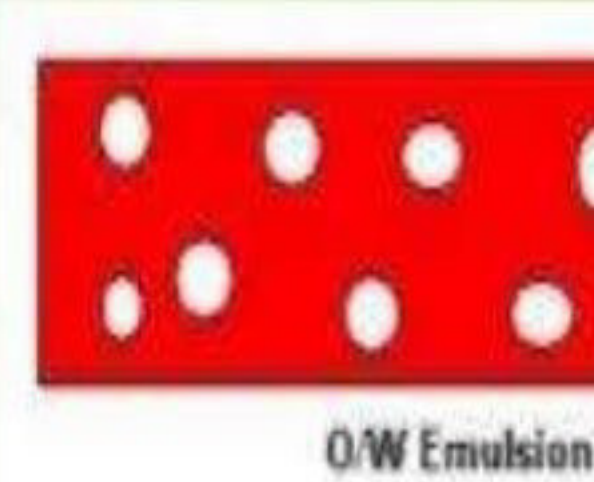
In this test,an assembly is used in which a pair of electrodes connected to an electric bulb is dipped into an emulsion.If the emulsion is o/w type,the electric bulb glows.

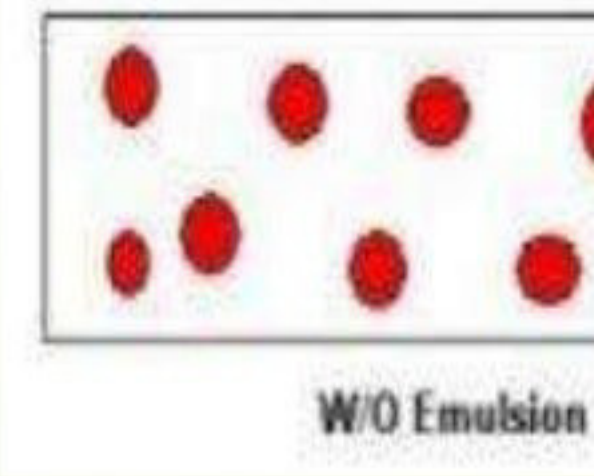


3.DYE TEST:-

When an emulsion is mixed with a water soluble dye such as amaranth and observed under the microscope.

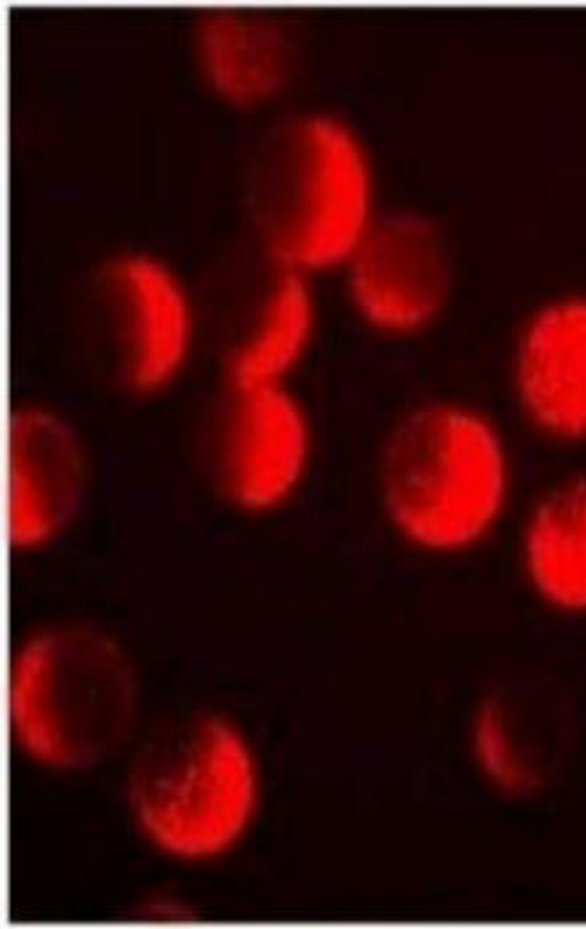
- If the continuous phase appears red,then it means that the emulsion is o/w type as water is the external phase.
- If the scattered globules appear red and continuous phase is colourless,then it is w/o type.





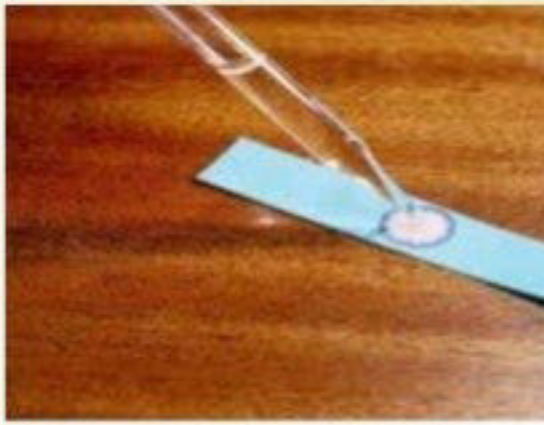
4.FLUORESCENCE TEST:-

Oil gives fluorescence under UV light,while water doesn't.Therefore,o/w emulsion shows spotty pattern when observed under UV,while w/o emulsion fluoresces.



5.COBALT CHLORIDE TEST:-

When a filter paper soaked in cobalt chloride solution is dipped into an emulsion and dried,it turns from blue to pink,indicating that the emulsion is o/w type.



Blue cobalt-chloride pa turning pink in the pre of water

PREPARATION OF EMULSIONS:-

The emulsions are prepared by two methods:-

1. Small scale method

a)Dry gum method

b)Wet gum method

c)Bottle method.

2. Large scale method.

EVALUATION OF EMULSIONS:-

1. Size distribution analysis.
2. Rate of phase separation.
3. Viscosity & rheological study.
4. Measurement of dielectric constant.
5. Conductivity measurement.
6. Influence of temperature.
7. Microwave radiation.
8. Microelectrophoretic measurement.

STABILITY OF EMULSIONS:-

The following three changes usually occurs during the storage of emulsion:-

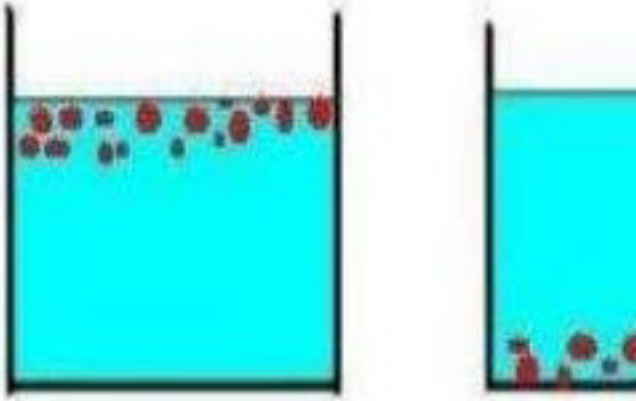
1. Creaming.
2. Cracking.
3. Phase inversion.

1.CREAMING:-

Creaming may be defined as the upward movement of dispersed globules to form a thick layer at the surface of emulsion.

The creaming depends on "Stokes law",the r of creaming depends on the various factors.

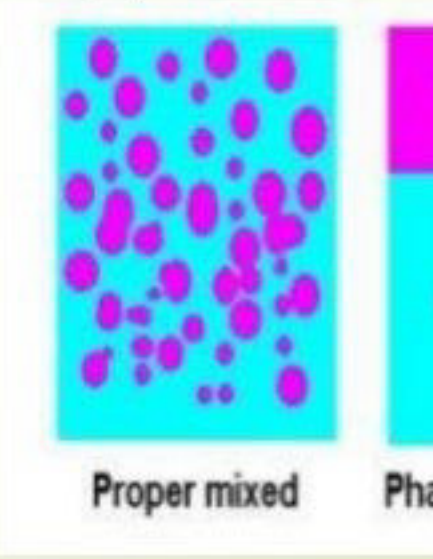
$$V=2r^2(d_1-d_2)g/9n$$



2.CRACKING:-

Cracking means the separation of two layers od ispersed phase and continuous phase due to coalescen ispersed phase globules.Cracking may be due to the llowing reasons:-

- By addition of emulsifying agent of opposite type.
- By decomposition of emulsifying agent.
- By addition of common solvent.
- By micro organisms.
- Changes in temperature.



3.PHASE INVERSION:-

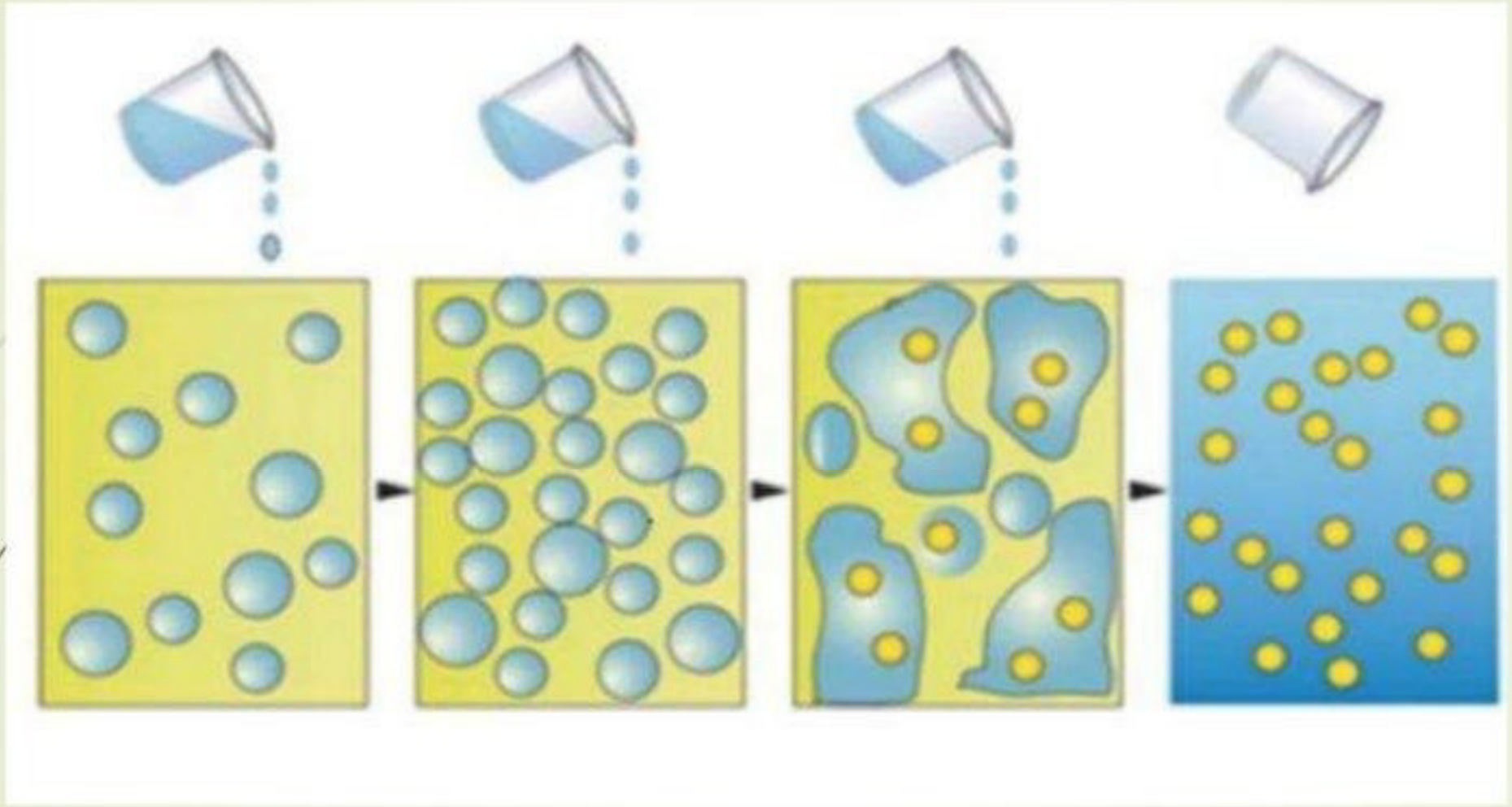
Phase inversion means change of one type of emulsion into the other type i.e., o/w emulsion changes into w/o type and vice versa.It may be due following reasons:-

a)By the addition of an electrolyte.

b)By changing the phase volume ratio.

c)By temperature change.

d)By changing the emulsifying agent.

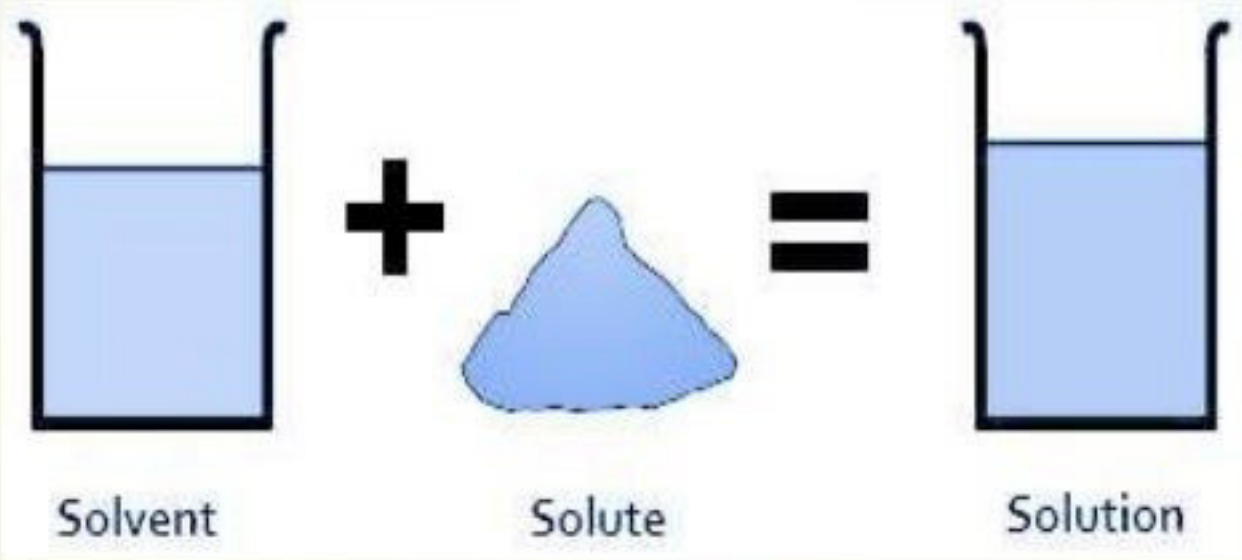


Phase inversion

SOLUTIONS

DEFINITION:-

In pharmaceutical terms,solutions are liquid preparations that contain one or more chemical substances dissolved in a suitable solvent or mixture mutually miscible solvents.



ADVANTAGES:-

1. Drug available immediately for absorption i.e., bioavailability of solutions is greater than that of oral solid dosage forms.
2. Flexible dosing.
3. Designed for oral route of administration.
4. No need to shake container.
5. Facilitates swallowing in difficult cases.

DISADVANTAGES:-

1. Drug stability reduced in solutions.
2. Bulky,difficult to transport and prone to container breakages.
3. Technical accuracy needed to measure dose on administration.
4. Measuring device is needed for administration.
5. Some drugs are poorly soluble.

CLASSIFICATION OF SOLUTIONS:-

- Oral solutions
- Oral syrups
- Oral elixirs
- Linctus
- Mouth washes/gargles

1.ORAL SOLUTIONS:-

- Oral solutions are administered to the GIT to provide absorption of the therapeutic agent.
- Oral solutions formulated over a broad p^H range due to the flexibility of GI environment.
- The usual p^H of oral solutions is about 7.0,unless there are issues regarding the solubility or stability of drugs.

2.ORAL SYRUPS:-

Syrups are highly concentrated aqueous solutions of sugar or a sugar substitute that contain a flavouring agent.

Eg:-Cherry syrup,orange syrup,raspberry syrup.

3.ORAL ELIXIRS:-

Elixir is a clear,hydroalcoholic solutions ormulated for oral use.The presence of lcohol in elixirs cause a problem in aediatric formulations and for adults who vish to avoid alvohol.It usually contains:-

- Purified water
- Alcohol
- Polyol cosolvents

4.LINCTUS:-

- A liquid oral preparation used for a demulcent,expectorant or sedative effect in treatment of cough.
- Linctuses are viscous preparations that contain the therapeutic agent dissolved in a vehicle composed of a high percentage of sucrose or other sweetening agents.
- Primarily employed for the treatment of cough,due to their soothing actions on the inflammed mucous membranes.

5.MOUTH WASHES/GARGLES:-

- These are designed for the treatment of infections and inflammation of the oral cavity.
- Formulations designed for this purpose employ water as the vehicle,although a cosolvent (alcohol) may be employed to solubilize the active agent.
- They include preservatives,colouring and flavouring agents and sweetening agents.

STABILITY OF SOLUTIONS:-

Both the chemical and physical stability of solution in their container are important.A solution must retain it's initia clarity,colour,odour,taste and viscosity over it's allocated shel life.

Major signs of instability are:-

1. Colour change
2. Precipitation
3. Microbial growth
4. Chemical gas formation.


Thank
you

TABLETS

Mr. Rajesh. M. Kuwar
(Department of Pharmaceutics)
JES's College of Pharmacy, Nandurbar

CONTENT.....

- Introduction
- General Properties
- Advantages
- Disadvantages
- Types of Tablets
- Tablet Additives

Continued....

ormulation Development

- Preformulation of drugs & additives
- Introduction to tablet Additives
- Need of Granulation
- Mechanisms
- Manufacturing Processes and Equipments for granula
- Advance Granulation Techniques
- Characterization and Evaluation

All about Tablets.

All about Tablet Coating

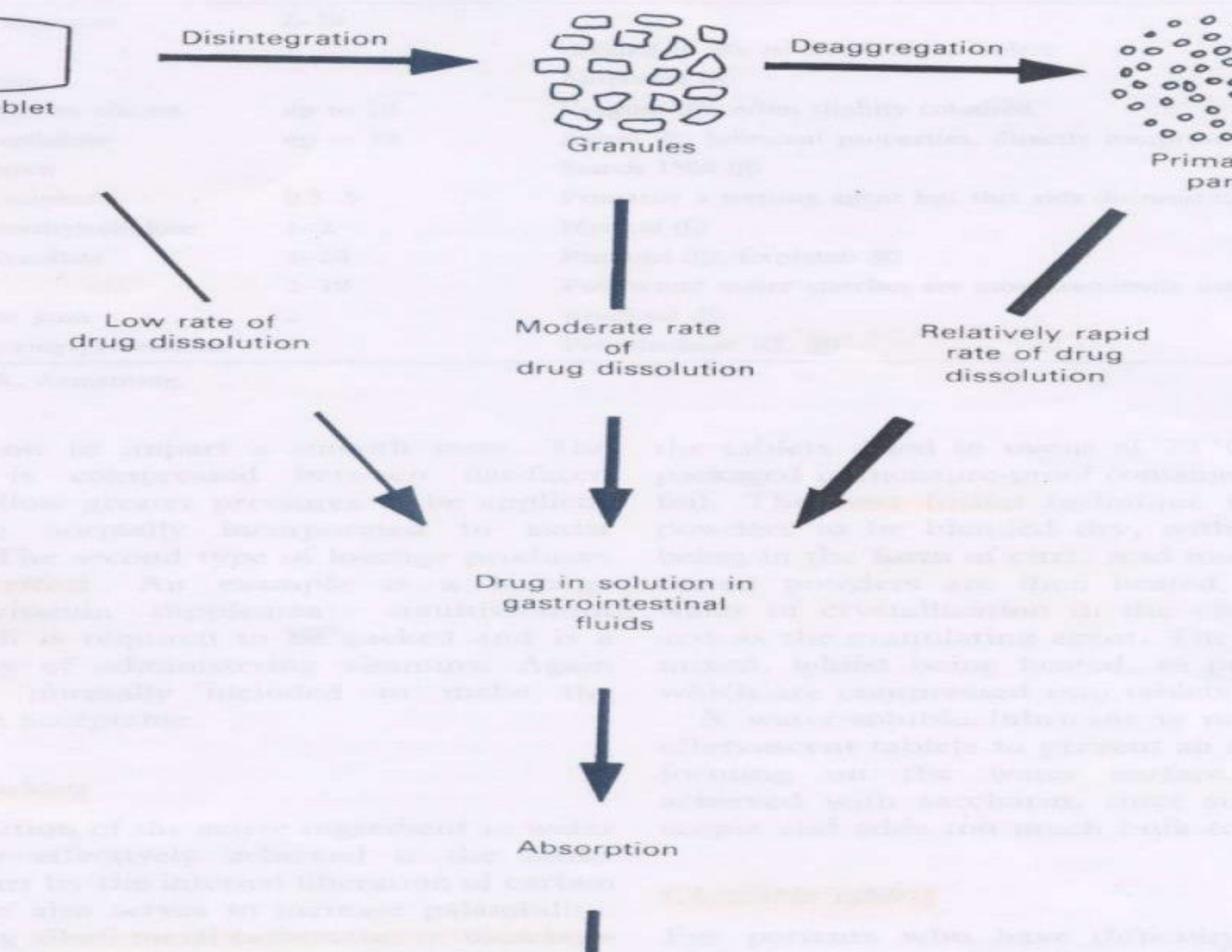
Introduction

Definition:

blet is defined as a compressed unit solid dosage form ntaining medicaments with or without excipients.

cording to the Indian Pharmacopoeia,
armaceutical tablets are solid, flat or biconvex dishes, unit sage form, prepared by compressing a drugs or a mixture of ugs, with or without diluents.

ey vary in shape and differ greatly in size and weight, pending on amount of medicinal substances and the intended ode of administration.


blet
Disintegration
Granules
Deaggregation
Prima
par
Low rate of
drug dissolution
Moderate rate
of
drug dissolution
Relatively rapid
rate of drug
dissolution
Drug in solution in
gastrointestinal
fluids
Absorption

➢ Advantages

reatest dose precision and the least content variabil

ost is lowest of all oral dosage form.

ghter and compact.

siest and cheapest to package and strip.

sy to swallowing with least tendency for hang-up.

tinued...

Sustained release product is possible by various techniques.

Objectionable odour and bitter taste can be masked by various techniques.

Suitable for large scale production.

Greatest chemical and microbial stability over all oral dosage fo

Product identification is easy and rapid requiring no additional

when employing an embossed and/or monogrammed punch fac

Disadvantages

icult to swallow in case of children and unconscious patients.

e drugs resist compression into dense compacts, owing to amo
, low density character.

gs with poor wetting, slow dissolution properties, may be diffi
late or manufacture as a tablet that will still provide adequate or fu
ilability.

r testing drugs, drugs with an objectionable odor or drugs that are se
gen may require encapsulation or coating. In such cases, capsule ma

General properties of Tablet dosage forms

let should have elegant product identity while free of defects like chips, cracl

ration, and contamination.

ld have sufficient strength to withstand mechanical shock during its productio

ing, shipping and dispensing.

ld have the chemical and physical stability to maintain its physical attributes

ablet must be able to release the medicinal agents in a predictable and reprod

.

have a chemical stability over time so as not to follow alteration of the medi

Tablets ingested orally:

- Compressed tablet, e.g. Paracetamol tablet
- Multiple compressed tablet
- Delayed release tablet, e.g. Enteric coated Bisacodyl tablet
- Sugar coated tablet, e.g. Multivitamin tablet
- Film coated tablet, e.g. Metronidazole tablet
- Chewable tablet, e.g. Antacid tablet

Tablets used in oral cavity:

- Buccal tablet, e.g. Vitamin-c tablet
- Sublingual tablet, e.g. Vicks Menthol tablet
- Troches or lozenges

lets administered by other route:

- Implantation tablet
- Suppositories or Inserts, e.g. Clotrimazole tablet

blets used to prepare solution:

- Effervescent tablet, e.g. Dispirin tablet (Aspirin)
- Dispensing tablet, e.g. Enzyme tablet (Digiplex)
- Hypodermic tablet
- Tablet triturates e.g. Enzyme tablet (Digiplex)

Tablet Additives

ddition to active ingredients, tablet contains a number of inert materials
wn as additives or excipients. Different excipients are:

iluent

inder and adhesive

isintegrents

Lubricants and glidants

Coloring agents

Flavoring agents

Sweetening agents

uents are ***fillers*** used to make ***required bulk*** of the tablet when the drug dosag
nadequate to produce the bulk.
ondary reason is ***to provide better tablet properties*** such as ***improve cohe***
mit use of ***direct compression*** manufacturing or to ***promote flow***.
iluents should have following properties:

They must be non toxic

They must be commercially available in acceptable grade

There cost must be low

They must be physiologically inert

They must be physically & chemically stable by themselves & with the drug

They must be free from all microbial contamination.

They do not alter the **bioavailability of drug.**

Commonly used tablet diluents

Lactose-anhydrous and spray dried lactose

Directly compressed starch-Sta Rx 1500

Hydrolyzed starch-Emdex and Celutab

Microcrystalline cellulose-Avicel (PH 101and PH 102)

Dibasic calcium phosphate dehydrate

Calcium sulphate dihydrate

Mannitol

Sorbitol

Sucrose- Sugartab, DiPac, Nutab

Dextrose

inders and Adhesives:

materials are added either dry or in wet- form to form granules

cohesive compacts for directly compressed tablet.

ple: Acacia, tragacanth- Solution for 10-25% Conc.

Cellulose derivatives- Methyl cellulose, HPC, HPMC

Gelatin- 10-20% solution

Glucose- 50% solution

Polyvinylpyrrolidone (PVP)- 2% conc.

Starch paste-10-20% solution

Sodium alginate

Sorbitol

isintegrants:

ed to a tablet formulation to facilitate its breaking or disintegratio

ntact in water in the GIT.

mple: Starch- 5-20% of tablet weight.

Starch derivative – Primogel and Explotab (1-8%)

Clays- Veegum HV, bentonite 10% level in colored tablet only

lose

Cellulose derivatives- Ac- Di-Sol (sodium carboxy methyl cellu

Alginate

PVP (Polyvinylpyrrolidone), cross-linked

s up to ten fold within 30 seconds when contact water.

ple: Crosscarmellose- cross-linked cellulose,

Crosspovidone- cross-linked povidone (polymer),

Sodium starch glycolate- cross-linked starch.

cross-linked products swell upto 10 fold with in 30 seconds when in co
vater.

tion of disintegrant is added before granulation and a portion b
ession, which serve as **glidants or lubricant.**

ation of carbon dioxide in effervescent tablets is also one wa
egration

Lubricant and Glidants:

Lubricants are intended to prevent adhesion of the tablet material

he surface of dies and punches,

Glidants are intended **to promote flow of granules** or **powder mater**
y **reducing the friction between the particles.**

mple:

ubricants-

ic acid, Stearic acid salt - Stearic acid, Magnesium stearate, Talc, P
ethylene glycols), Surfactants

idants-

Starch – 5-10% conc., Talc-5% conc., Silica derivative - Colloidal silicas suc

e use of colors and dyes in a tablet has three purposes:

lasking of off color drugs

roduct Identification

roduction of more elegant product

l coloring agents must be approved and certified by FDA. Two forms of col
in tablet preparation – FD &C and D & C dyes. These dyes are applied as s
granulating agent or Lake form of these dyes. Lakes are dyes absorbed on h
and employed as dry powder coloring.

ample: FD & C yellow 6-sunset yellow

FD & C yellow 5- Tartrazine

FD & C green 3- Fast Green

FD & C blue 1- Brilliant Blue

FD & C blue 2 - Indigo carmine

avoring agents:

hewable tablet- flavor oil are used

veetening agents:

hewable tablets: Sugar, mannitol.

ccharine (artificial): 500 time's sweeter than sucrose

sadvantage: Bitter aftertaste and carcinogenic

partame (artificial)

advantage: Lack of stability in presence of moisture.

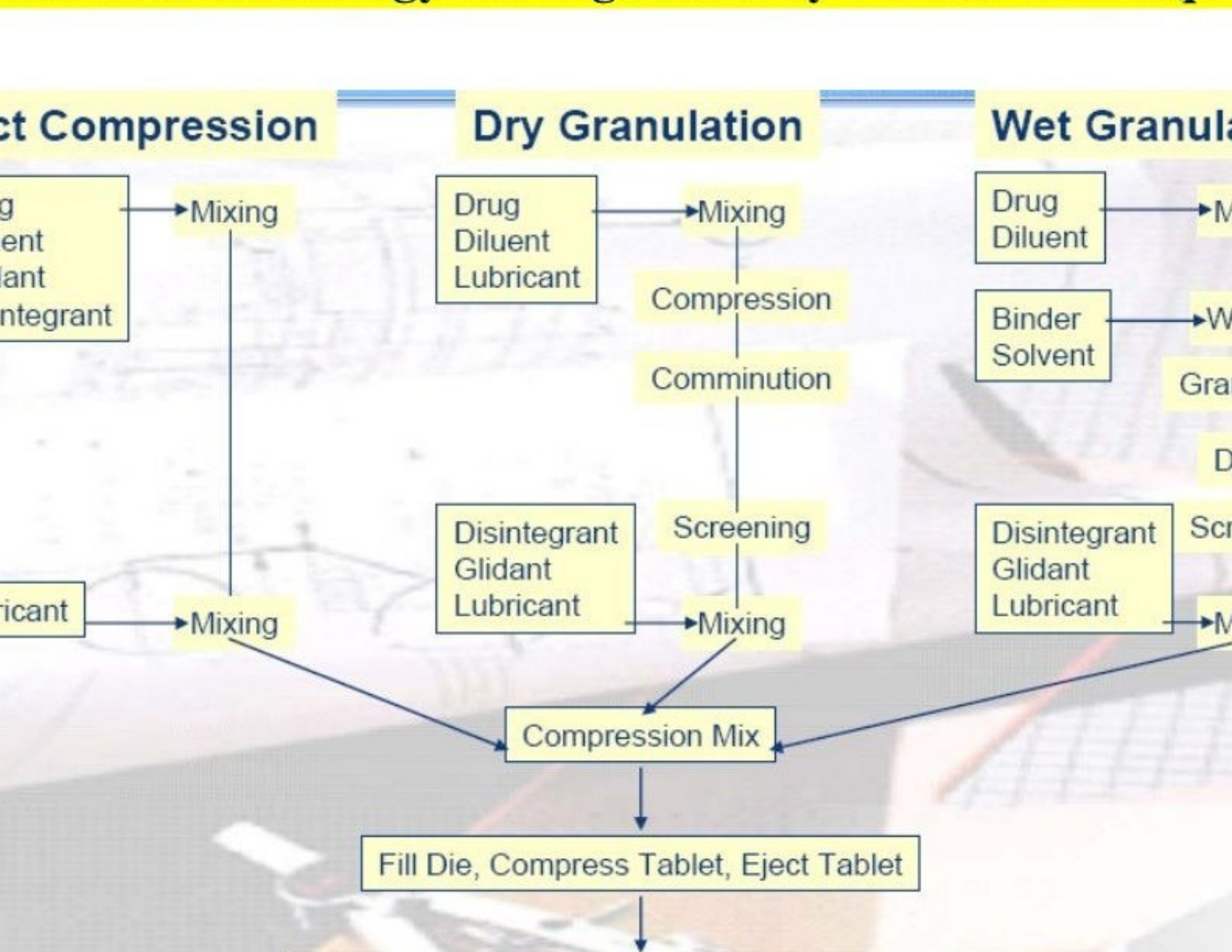
Granulation

Need

- To prevent segregation of the constituents of the powder mix
- To improve the flow properties of the mix
- To improve the compaction characteristics of the mix
- Other reasons: Toxic, Slightly hygroscopic, denser.

Methods

- Dry granulation
- Wet granulation


ct Compression
Dry Granulation
Wet Granula
g
ent
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ntegrant
Mixing
Drug
Diluent
Lubricant
Mixing
Compression
Comminution
Drug
Diluent
Binder
Solvent
Gra
D
Disintegrant
Glidant
Lubricant
Screening
Disintegrant
Glidant
Lubricant
Scr
ricant
Mixing
Mixing
Compression Mix
Fill Die, Compress Tablet, Eject Tablet

Mechanisms of Granulation

There are Five Particle Bonding Mechanisms,

dhesion and cohesion forces in the immobile liquid films

terfacial forces in mobile liquid films within the granules

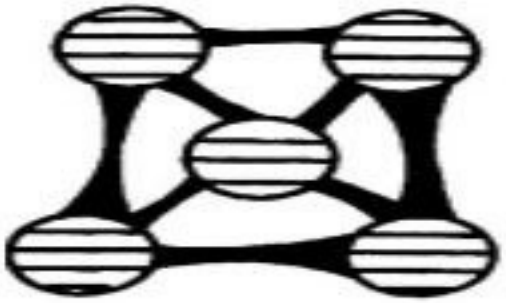
ormation of solid bridges after solvent evaporation

ttractive forces between solid particles

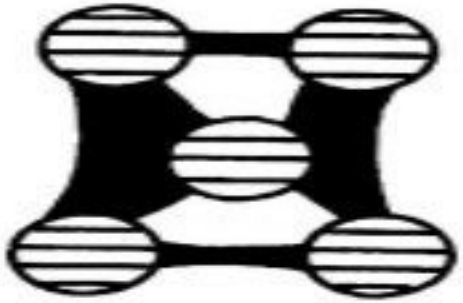
echanical interlocking

- ***Adhesion and cohesion forces in immobile liquid films*** between individual primary powder particles.

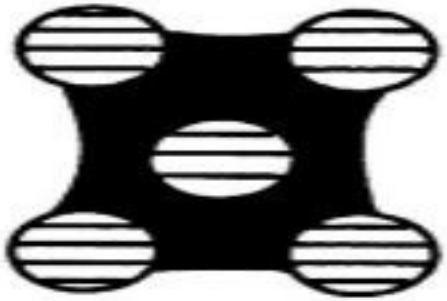
- ***Interfacial forces in mobile liquid films***



Pendular



Funicular



Capillary

Droplet

- ***Solid bridges***

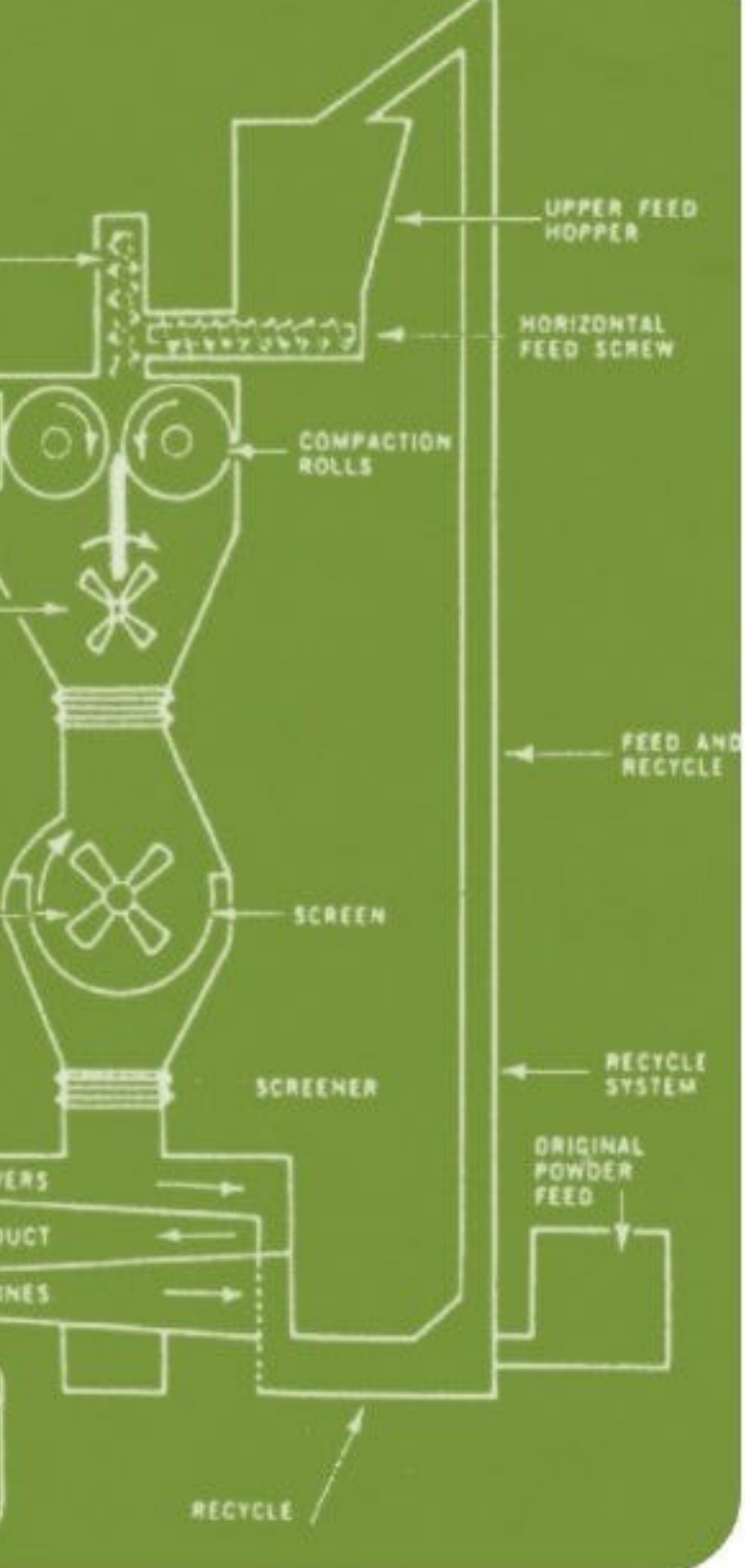
Partial mellting, Binder hardening, crystalization of dissolved sub.

- ***Attractive forces*** between ***solid particles***


Weighing
Mixing
Granulation
Screening
Drying
Screening
Lubrication

Granulation Equipments (Granulators)

- Dry granulator
- Wet granulator



❑ Dry granulators:

- **Sluggers**
- **Roller Compactors**

Is used when……

➢ Effective dose of drug is too hi

direct compression

➢ Drug is sensitive to heat or mo

or both.

Wet granulators

Shear mixer granulator

High speed granulator

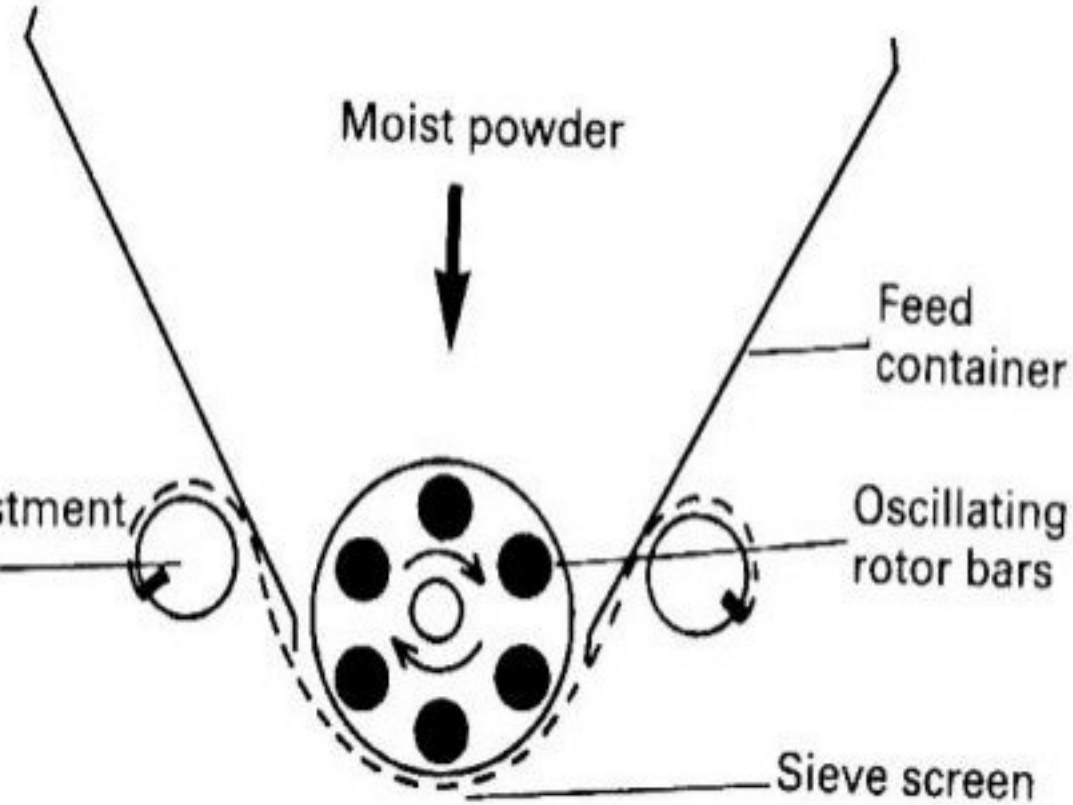
Fluidized bed granulator

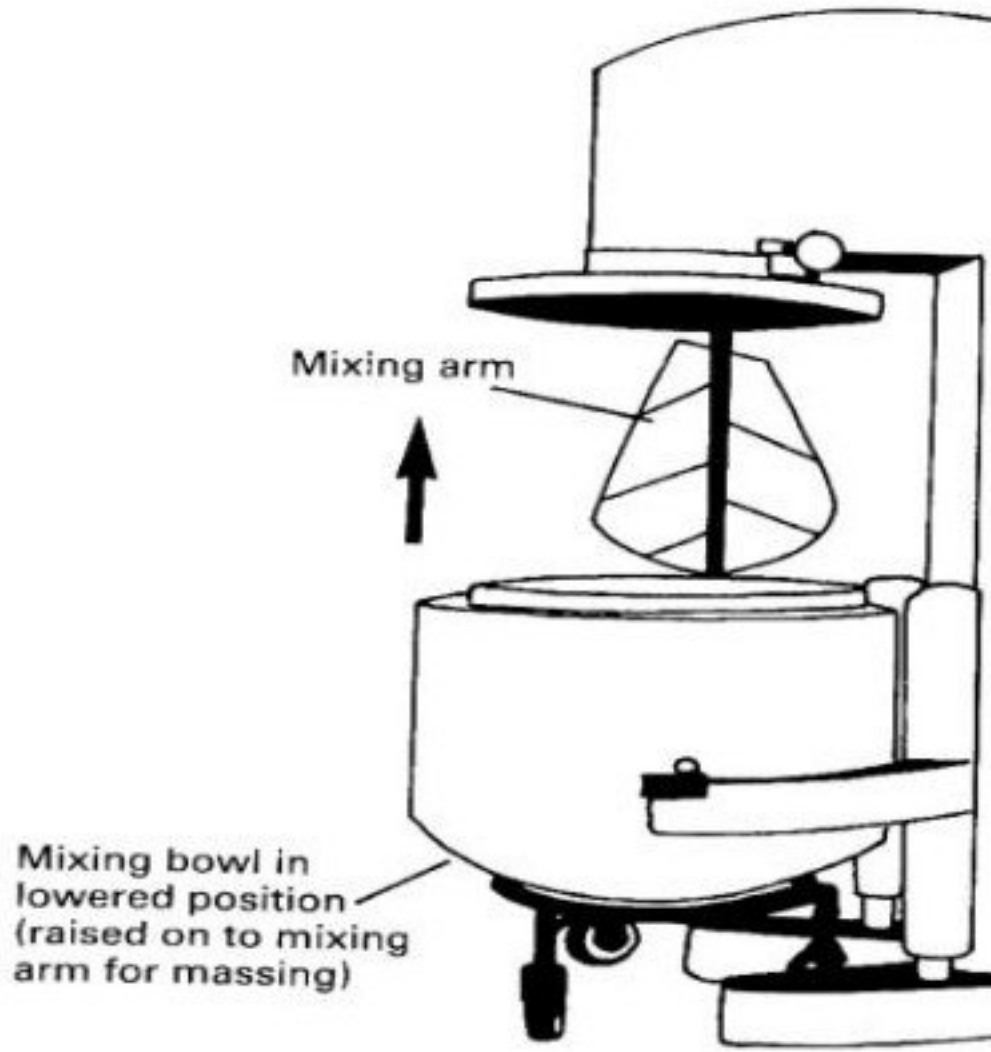
Spray driers

gh Shear anulator	Littleford Lodige Mixer/Granulato Littleford MGT Granulator Diosna Granulator Gral Mixer/Granulator
anulator with ying Facility	Fluidized Bed Granulator Day Nauta Mixer Processor Double cone/Twin Shell Processo Topo Granulator
ecial Granulator	Roto Granulator Marumerizer

Wet granulation equipment

- shear granulator





OP Of Shear Mixture Granulator

Mixed powder are fed in to the bowl

Granulating liquid is added

The moist mass has then transferred to a granulator such as oscillating granulator

Disadvantage

ong duration

arge number of equipment are needed

ligh material loss

Advantage

lot very sensitive to the material

nd point can be determined by inspection

High speed granulator

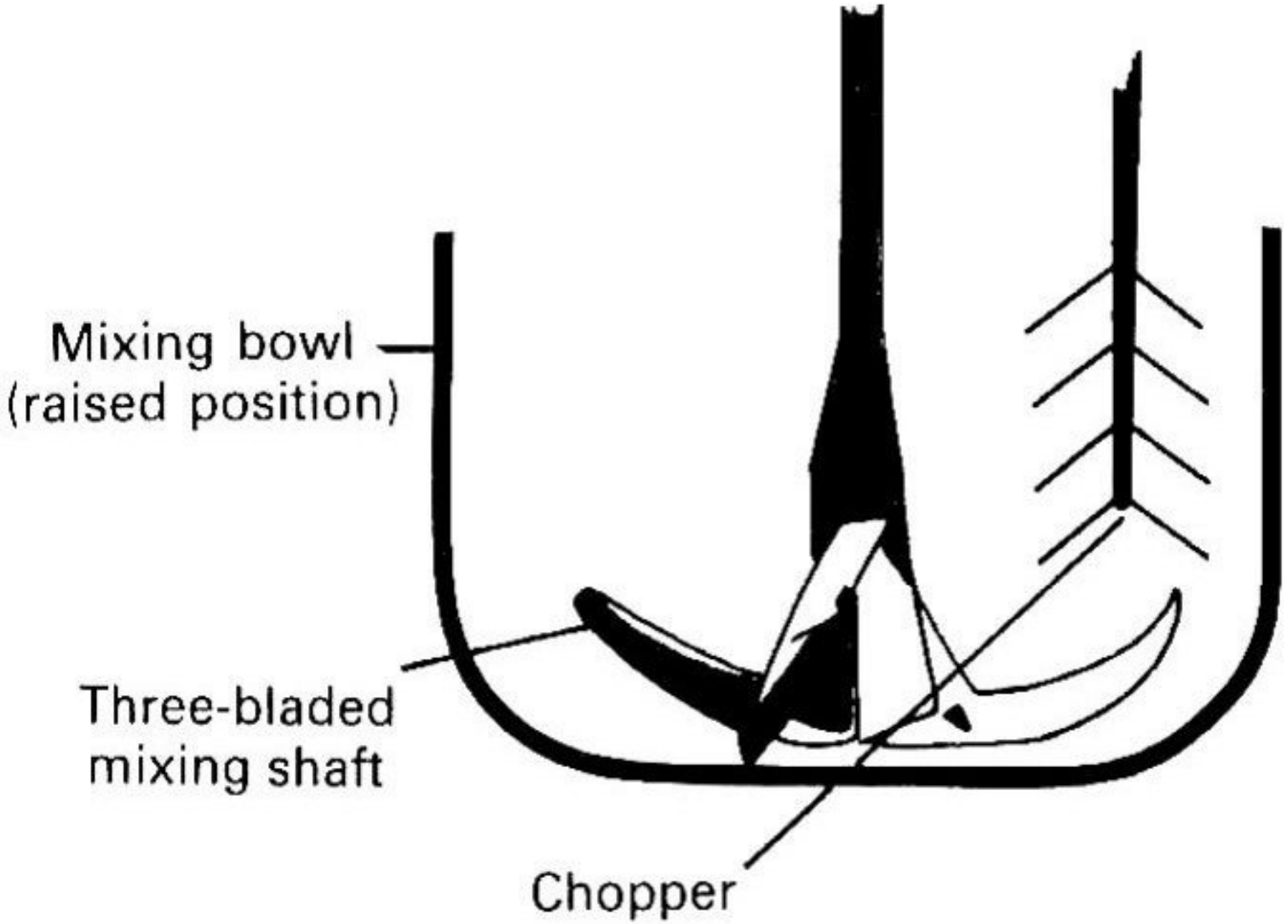
Widely used in pharmaceutical

SS mixing bowl containing a three blade main impeller, revolves in horizontal plane, and a three blade auxiliary chopper –revolves vertical or horizontal plane

Unmixed powder –in the bowl mixed for few minute with rotating impeller

Granulation

High speed granulator



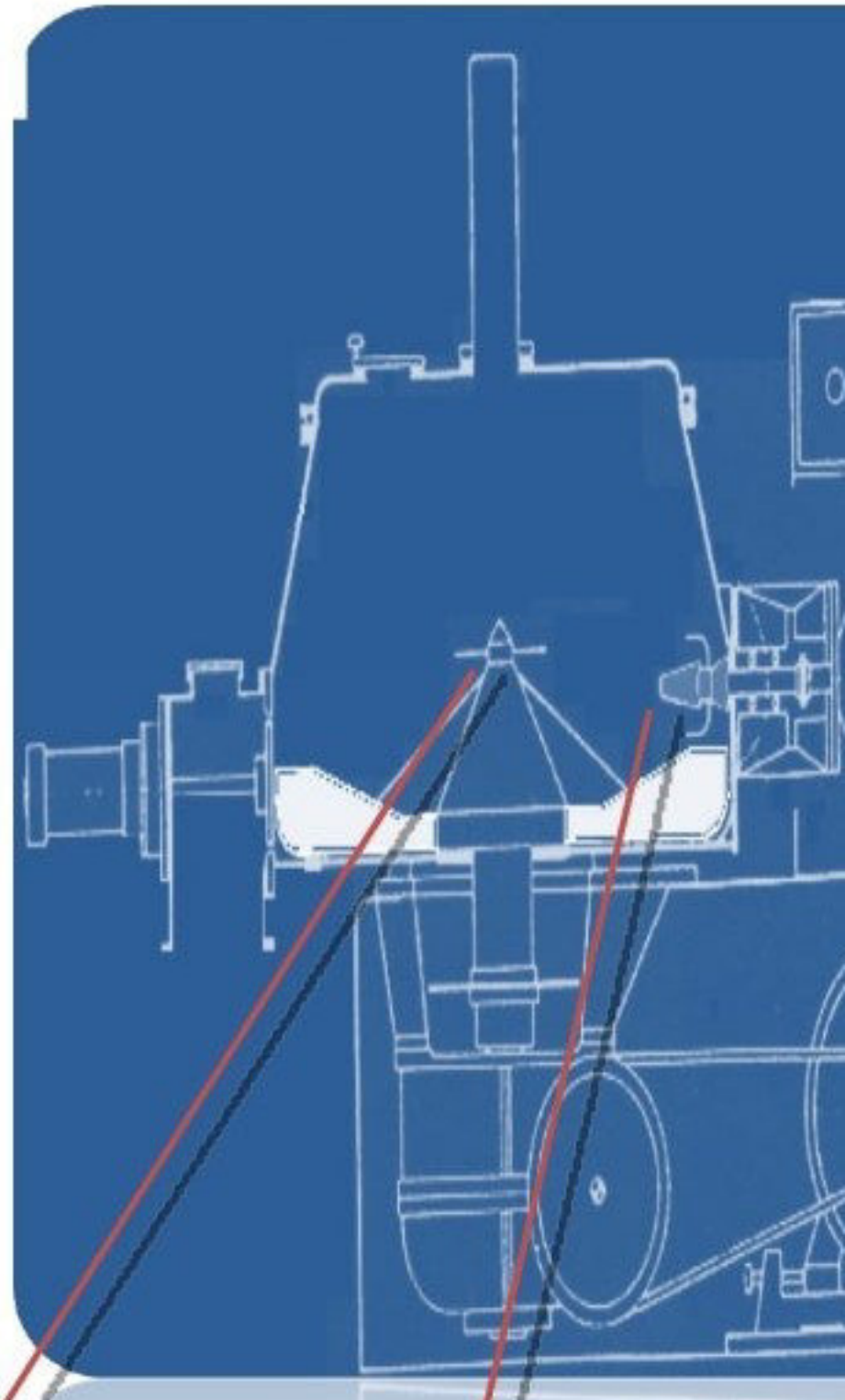
pid Mixer Granulator (RMG)

ves more normal PSD

h lesser fines.

pical Time Sequence

- Mixing – 2 minutes
- Granulation – 8 minutes
- Discharge – 1 minutes



Advantage

Mixing,Massing,Granulation in a single equipmen

within few minutes

Disadvantage

End point monitor needed

signs of FB granulators

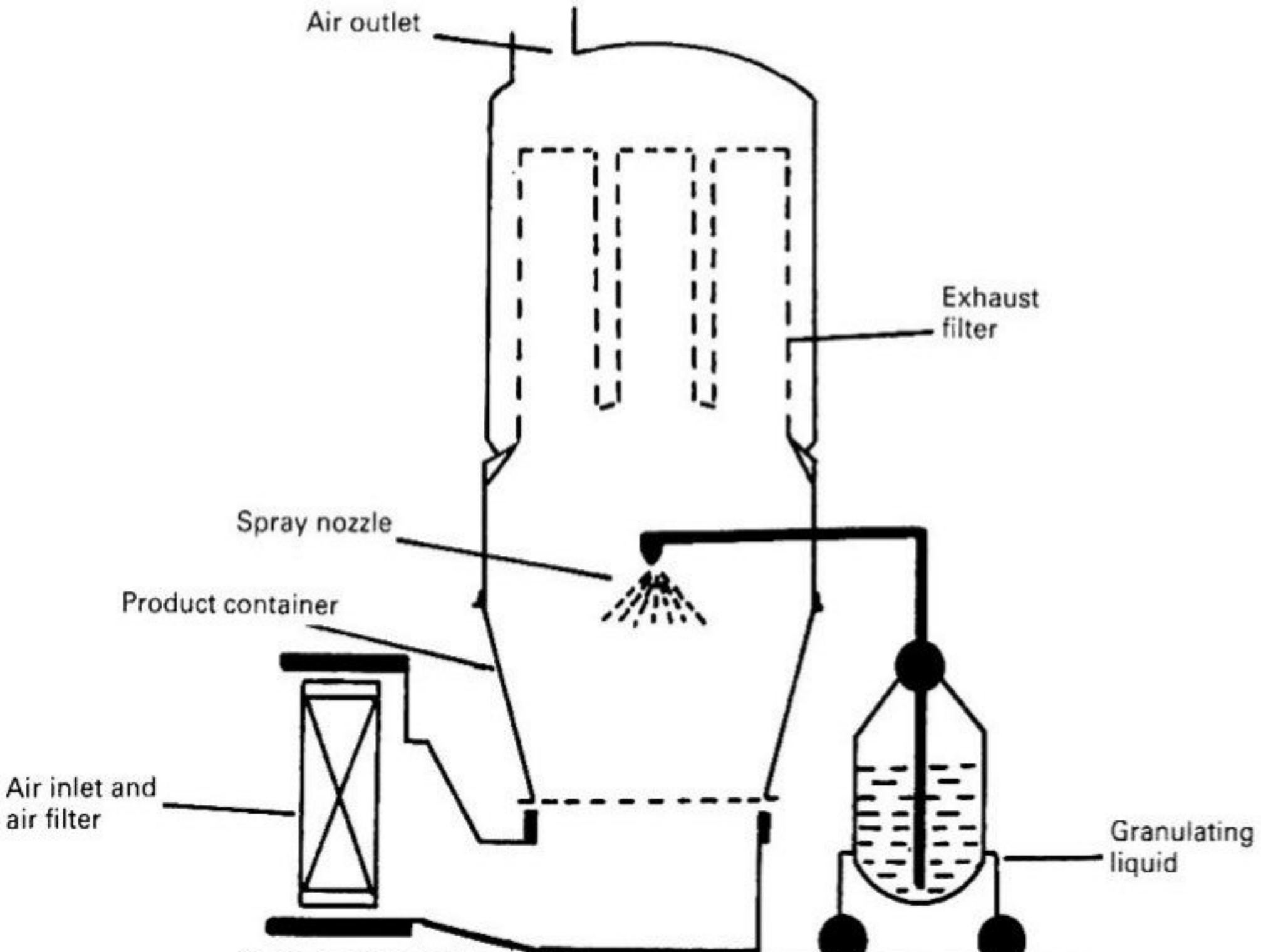
Top spray

Bottom spray

Rotating disc

granulator

Fluidized Bed Granulator



Fluidized Bed Granulator

dvantage

One unit so saving labour cost, transfer loses and time

2-6 time greater heat transfer than tray dryer

Uniform drying....prevent mottling.

Process can be automated once parameters optimized

isadvantage

Expensive

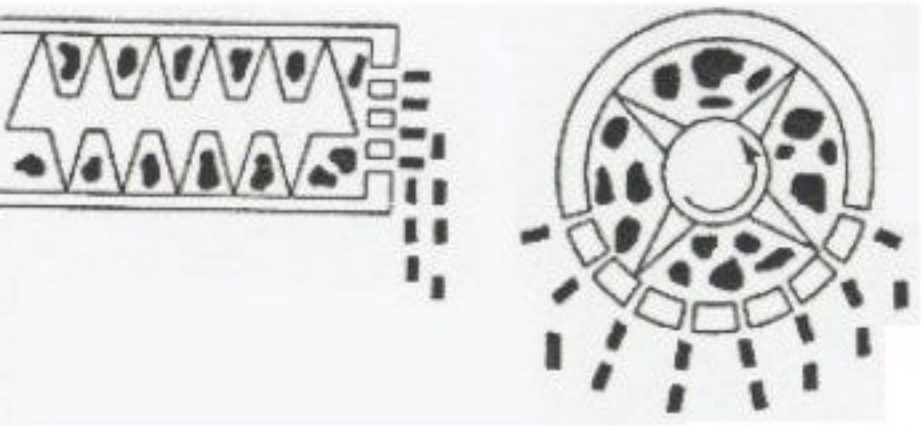
Multiple process variable

Filter clocking, demixing, electrostatic charge, solvent explosion

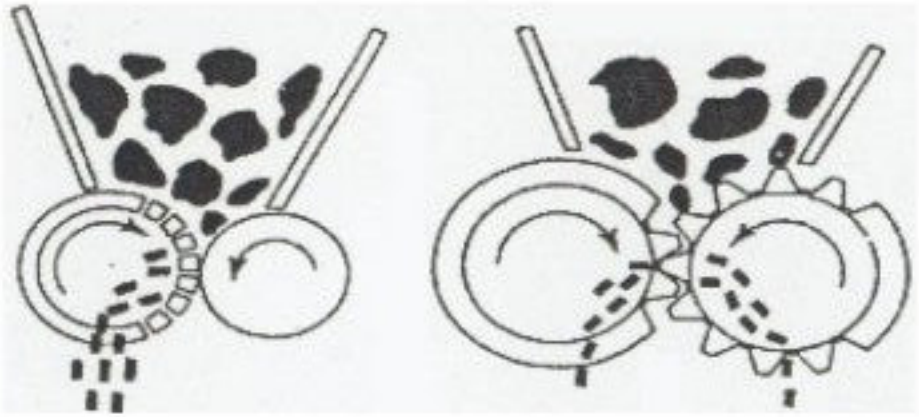
Fluidized Bed Granulator

(Industrial Equipment)

Wet mass containing *drug*, *diluents* and *binder* is pas
through extruder to get *rod* shaped segments.



Screw-feed Extruder



Cylinder

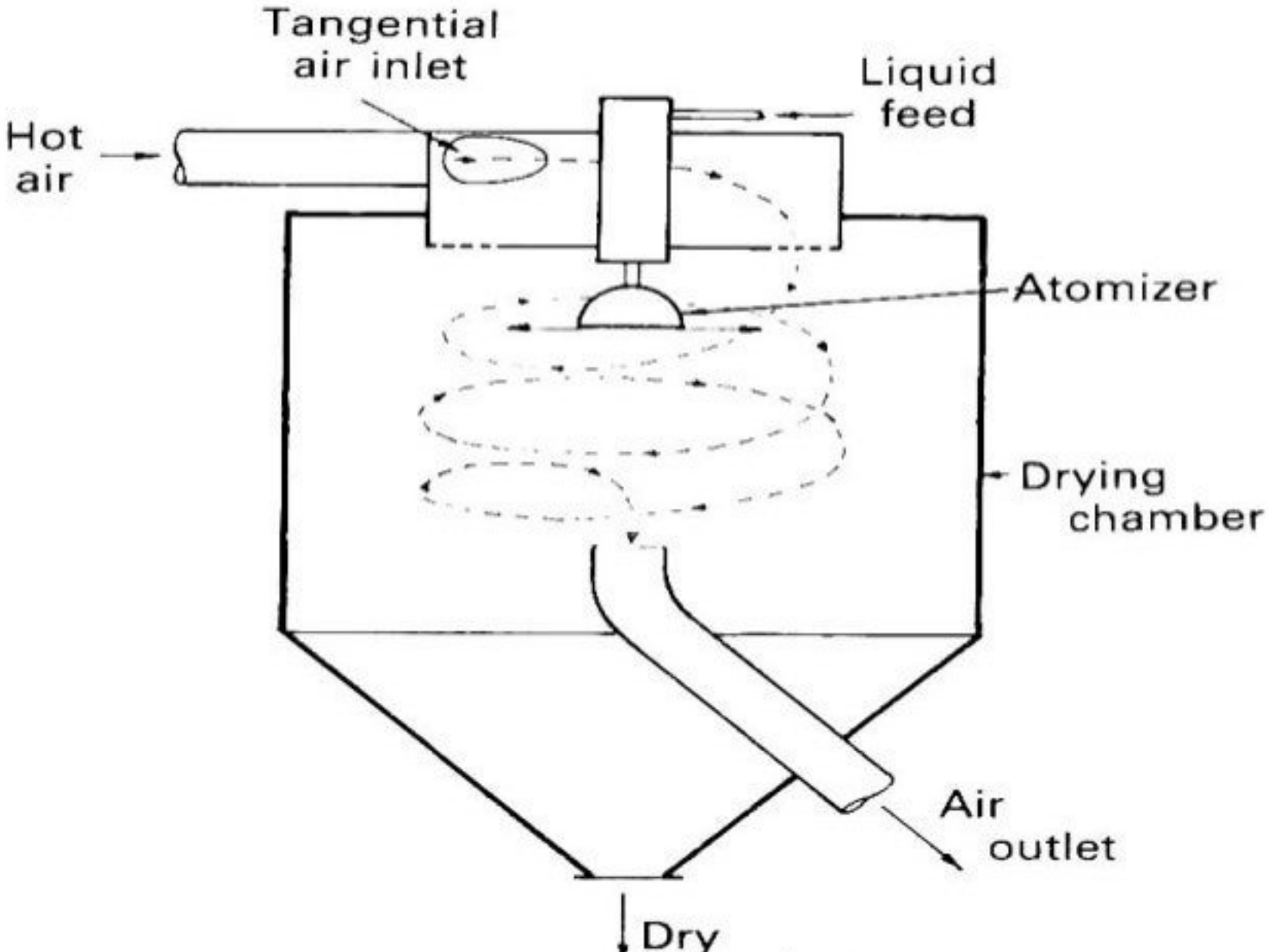
egments are placed in MERUMIZER where they are shape
here by centrifugal and frictional forces produced by rotat
ates/blades and form granules

Advantage

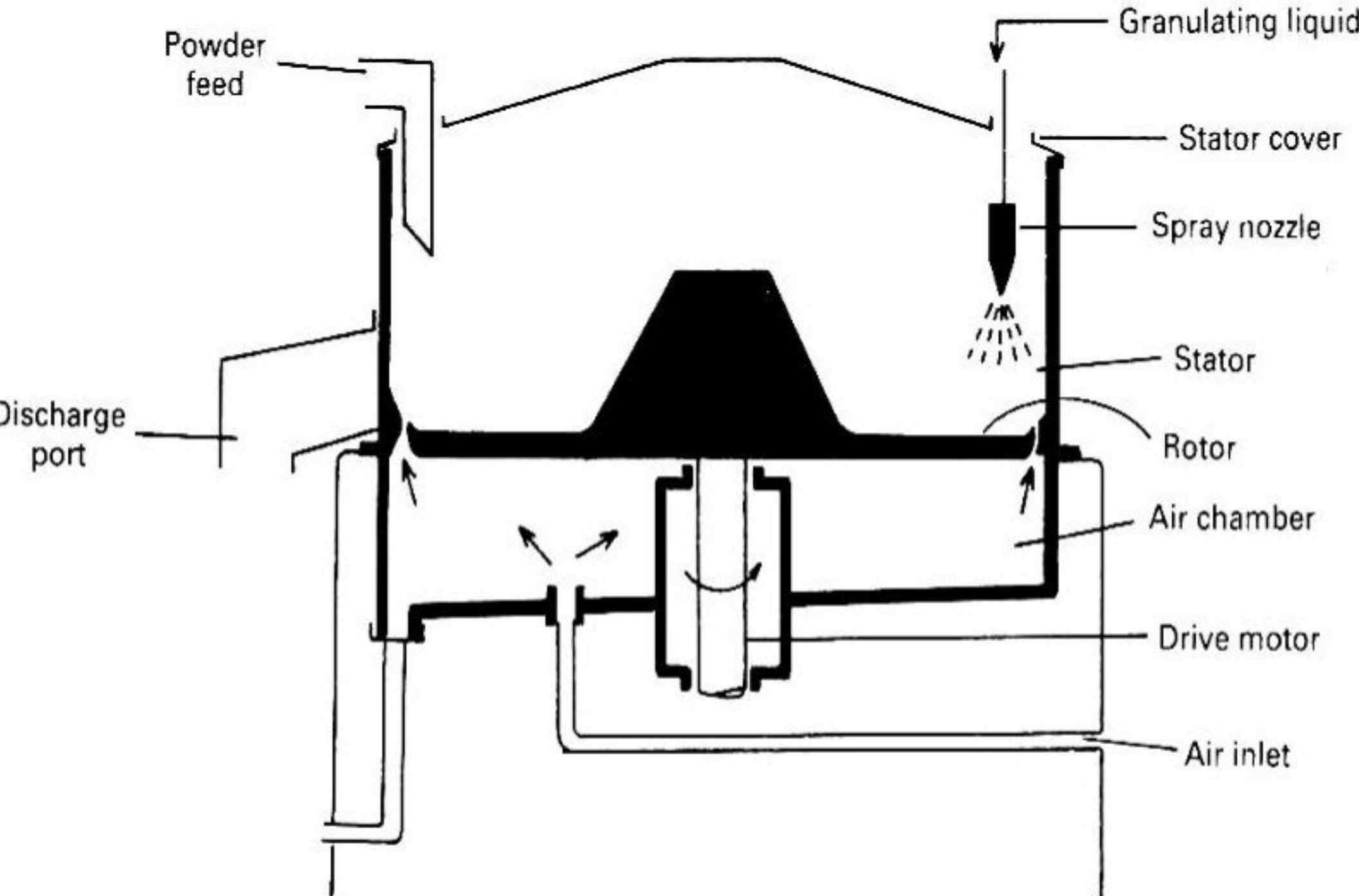
ranules with regular size, shape with lower friability,

Other More Specialized Granulators

- **Spray Driers**



Pelletizers



A melt granulation process has been investigated which efficiently agglomerates pharmaceutical powders for use in both immediate- and sustained-release solid dosage forms.

The process utilizes materials that are effective as granulating fluids when they are in the molten state.

Cooling of the agglomerated powders and the resultant solidification of the molten materials completes the granulation process.

Both the molten agglomeration and cooling solidification were accomplished in a high shear Collette Gral mixer equipped with a jacketed bowl.

Hence, the melt granulation process replaces the conventional granulation and drying operations which use water or alcohol

Need of other component

Large dose- not suitable

Small dose-impractical

Moderate dose- suitable

Directly compressible vehicles

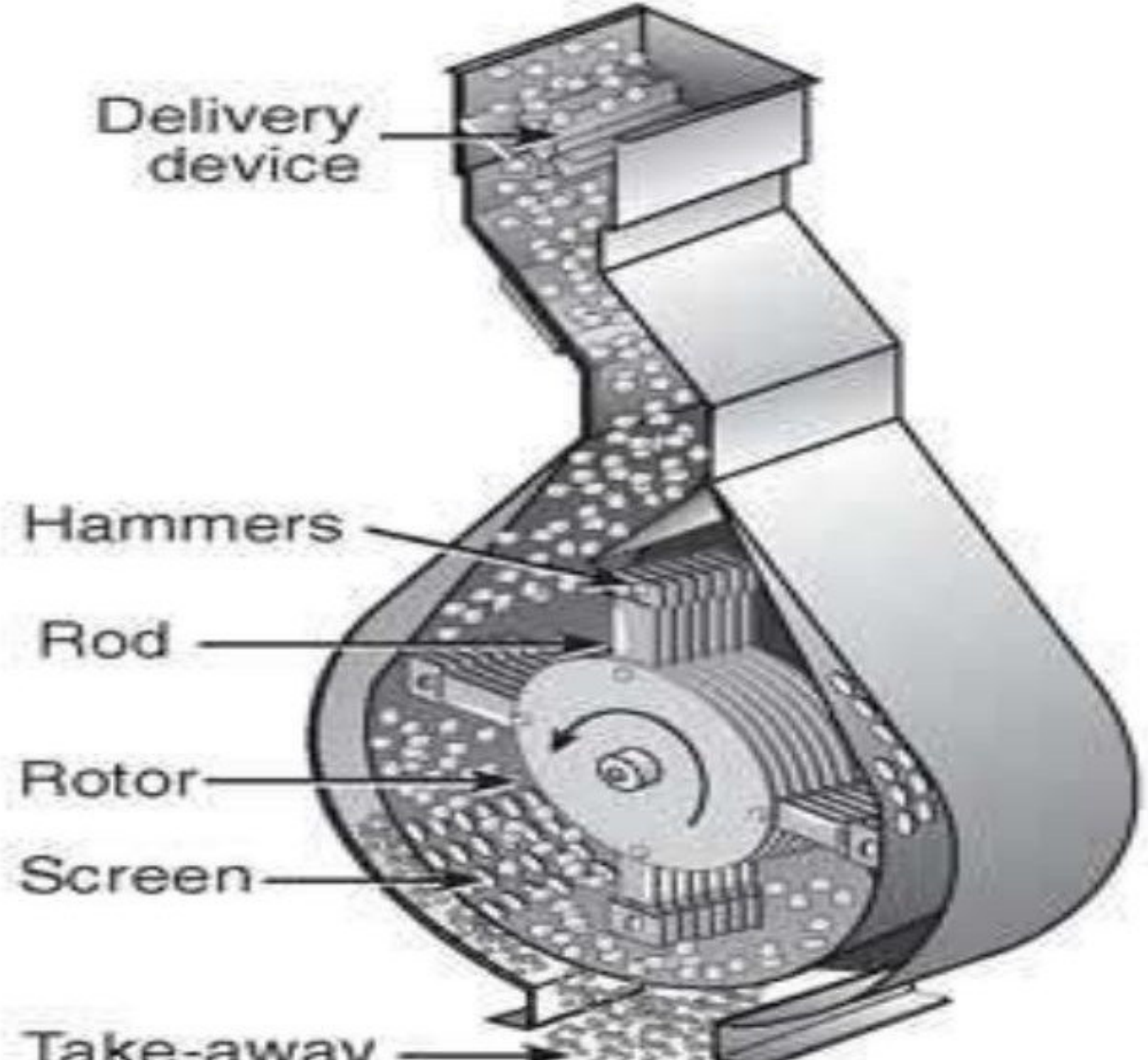
Limitations

1) Stratification-poor content uniformity
2) Large dose drugs [30%]
3) Interaction
4) Static charge

Equipment and procedures used

1) Screening/Milling
   * Three Parts
   * Principle
   * Operation
   * Types of Mills

Hammer Mill

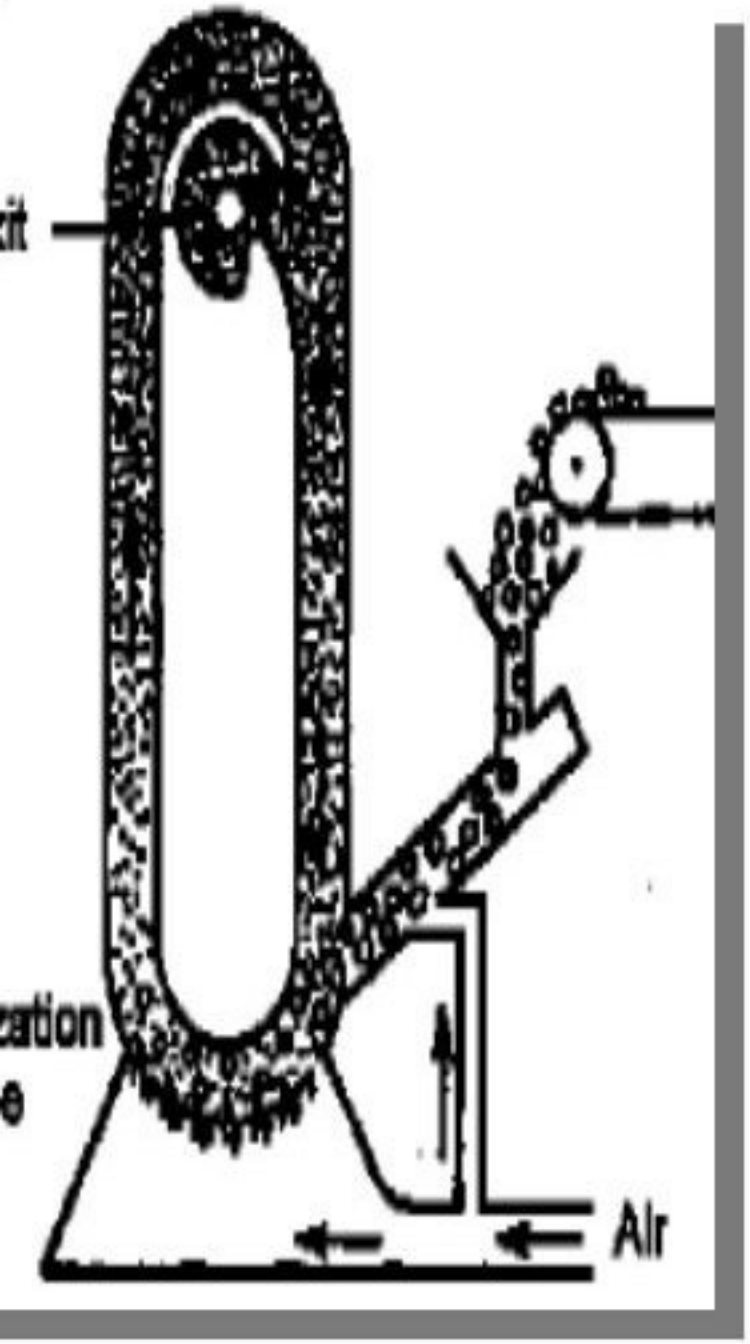


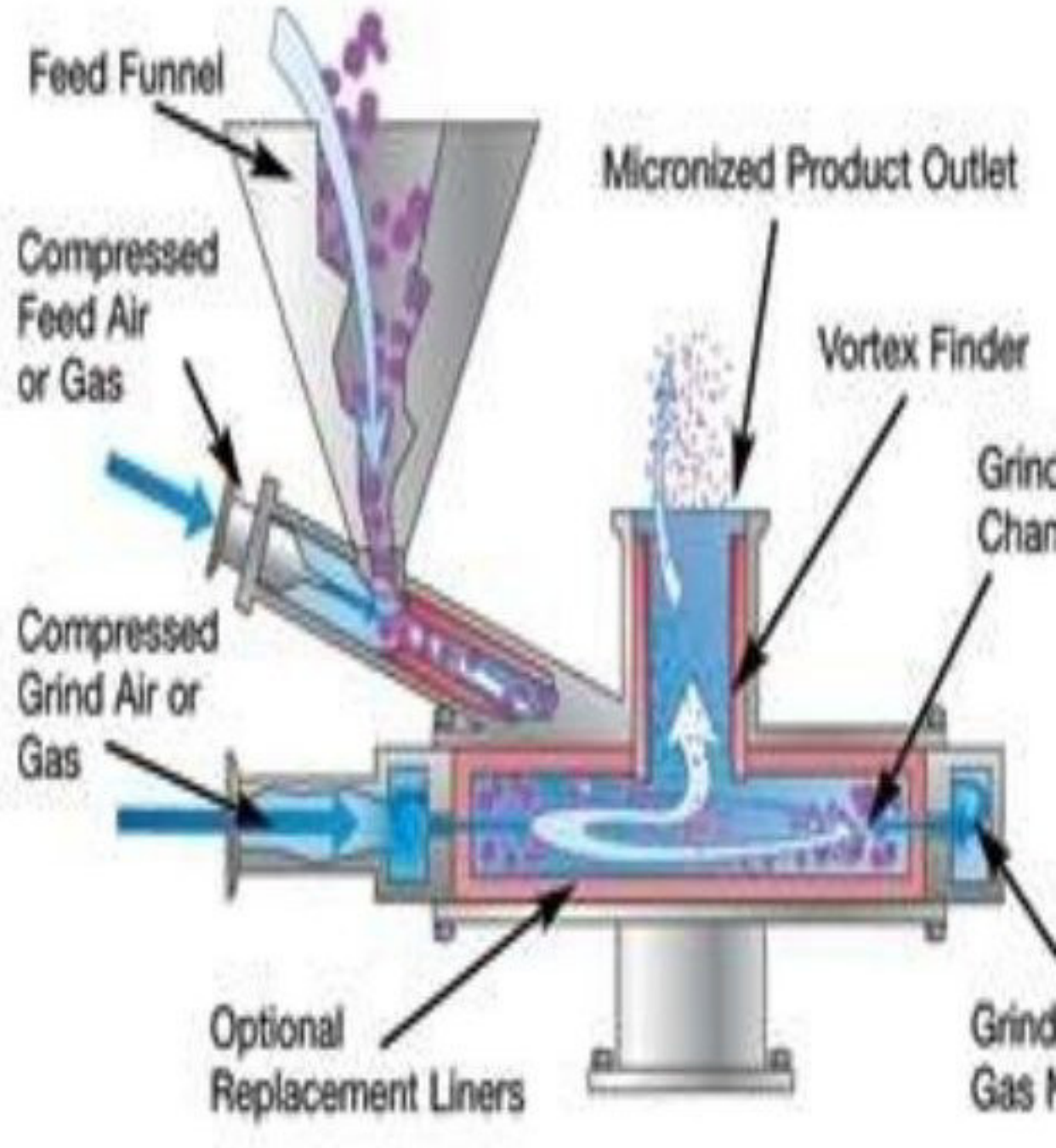
Ball Mill

Working Mechanism

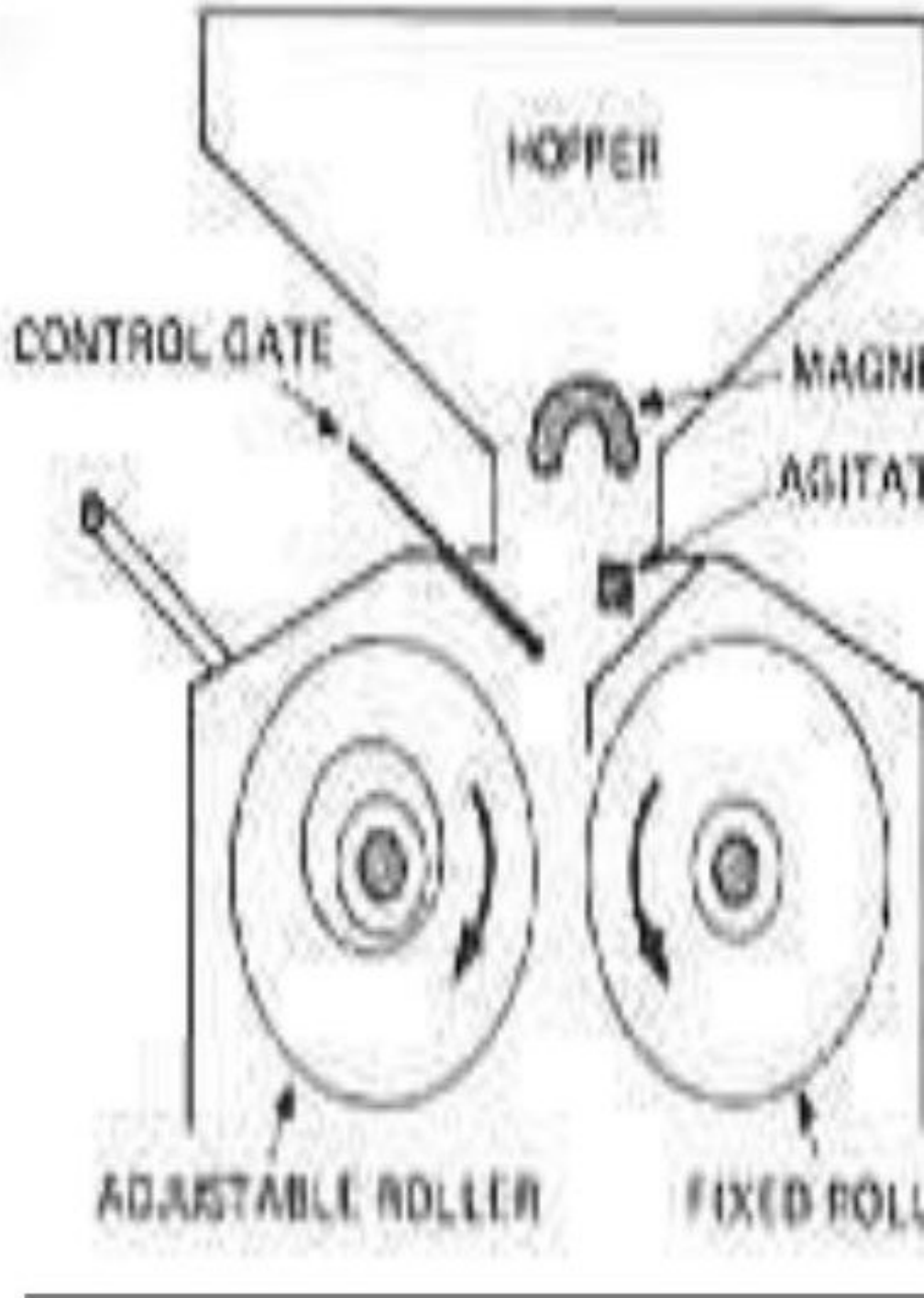
Industrial Model

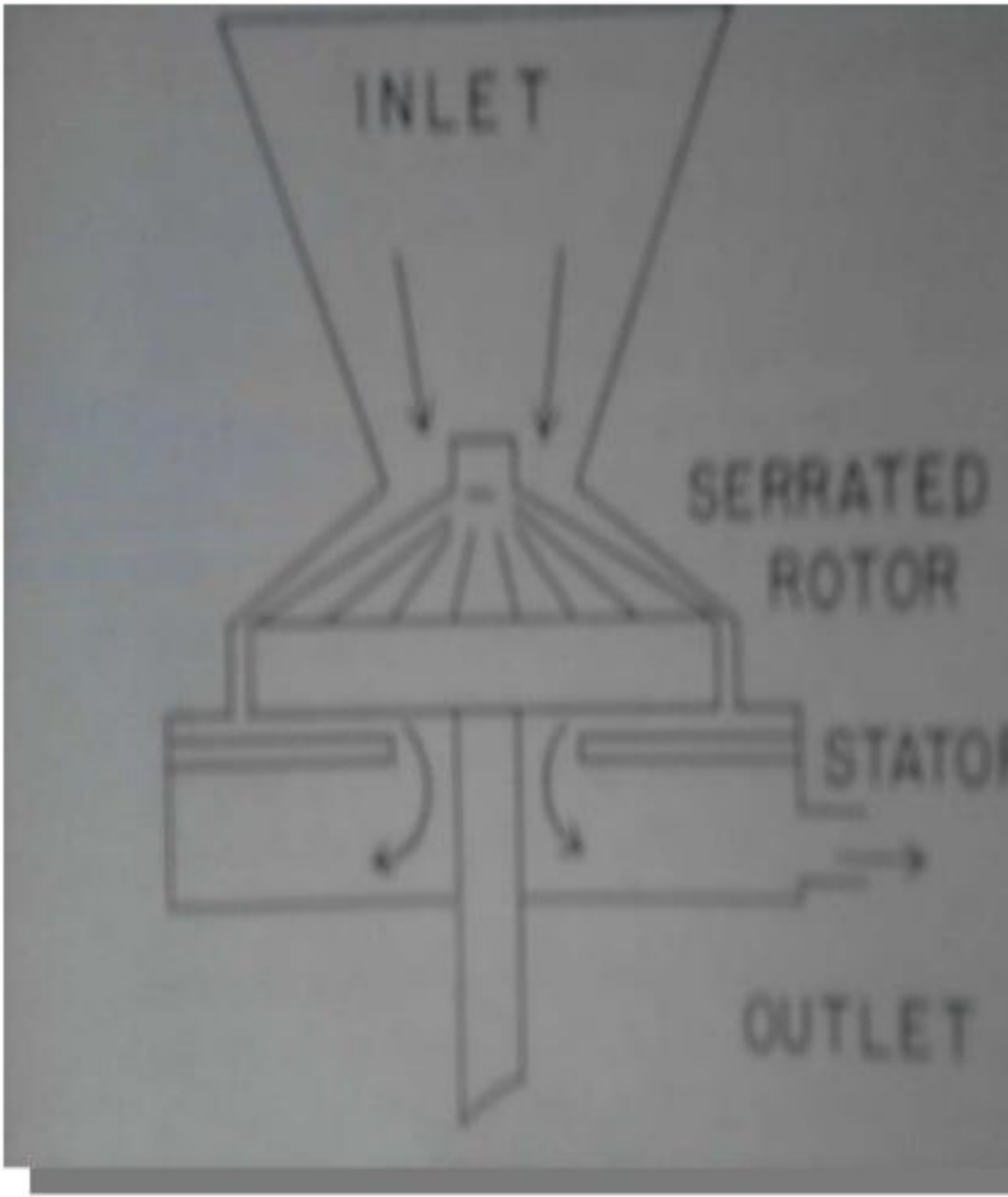
Fluid Energy Mill






Retsch


HOPPER
CONTROL GATE
ADJUSTABLE ROLLER


INLET
SERRATED
ROTOR
STATOR
OUTLET

Tablet Production

Powders intended for compression into tablets must po

two essential properties

Powder fluidity

- ✓ The material can be transported through the hopper into the die
- ✓ To produce tablets of a consistent weight
- ✓ Powder flow can be improved mechanically by the use of vibrators, incorporate the glidant

Powder compressibility

The property of forming a stable, intact compact mass wh

Tableting Procedure

- Filling
- Compression
- Ejection

Tablet Compression Machines

Hopper for holding and feeding granulatio to be compressed

Dies that define the size and shape of the tablet

Punches for compressing the granulation within the dies

Cam tracks for guiding the movement of punches

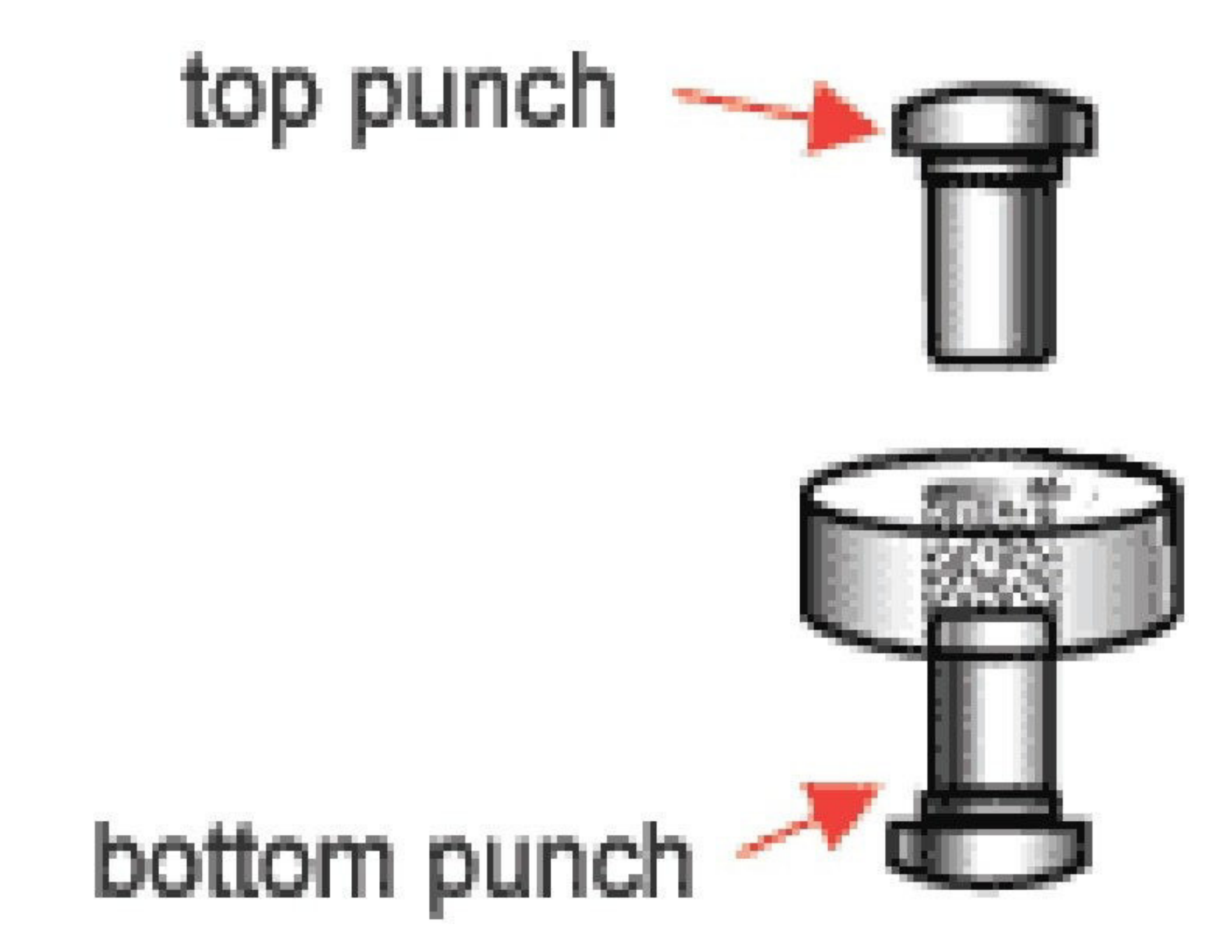
Feeding mechanisms for moving granulation from the hopper into the dies

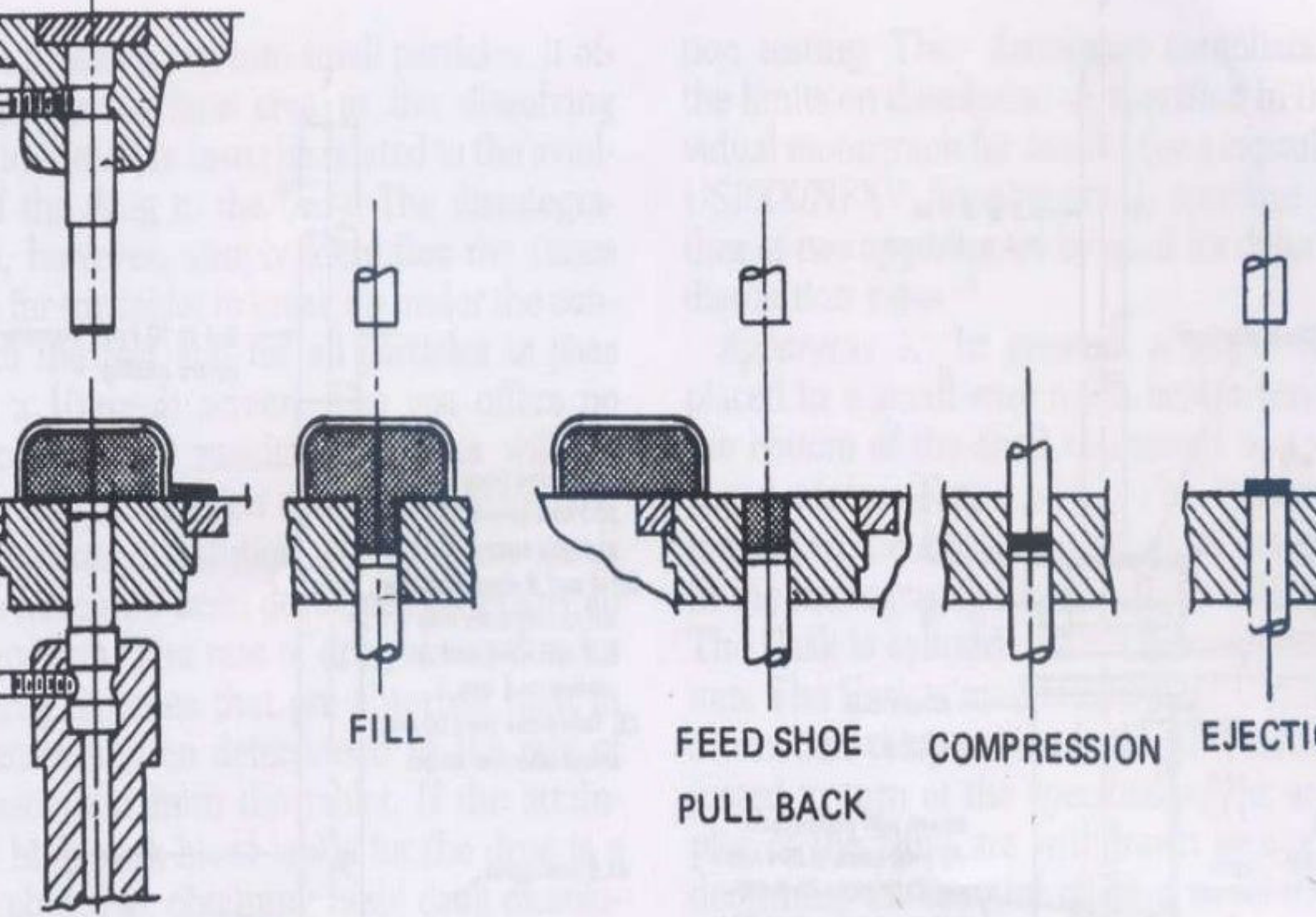
Single Punch Machine

The compression is applied by the upper punch

Stamping press

Single Punch Machine (Tablets)


top punch
bottom punch



5. *The compression cycle of a single-punch tablet press. (Courtesy of Vector Corporation, Marion, IA*

Multi-station Rotary Presses

The head of the tablet machine that holds the upper punche
ies and lower punches in place rotates

As the head rotates, the punches are guided up and down by
ixed **cam tracks**, which control the sequence of filling,
ompression and ejection.

The portions of the head that hold the upper and lower
unches are called the **upper an lower turrets**

The portion holding the dies is called the **die table**

The **pull down cam (C)** guides the lower punches to the bottom, allowing the dies to overfill

The punches then pass over a **weight-control cam (E)**, wh reduces the fill in the dies to the desired amount

A **swipe off blade (D)** at the end of the feed frame remove the excess granulation and directs it around the turret and into the front of the feed frame

hile simultaneously the upper punches ride beneath the

pper compression roll (G)

he upper punches enter a fixed distance into the dies, whil

e lower punches are raised to squeeze and compact the

anulation within the dies

fter the moment of compression, the upper punches are

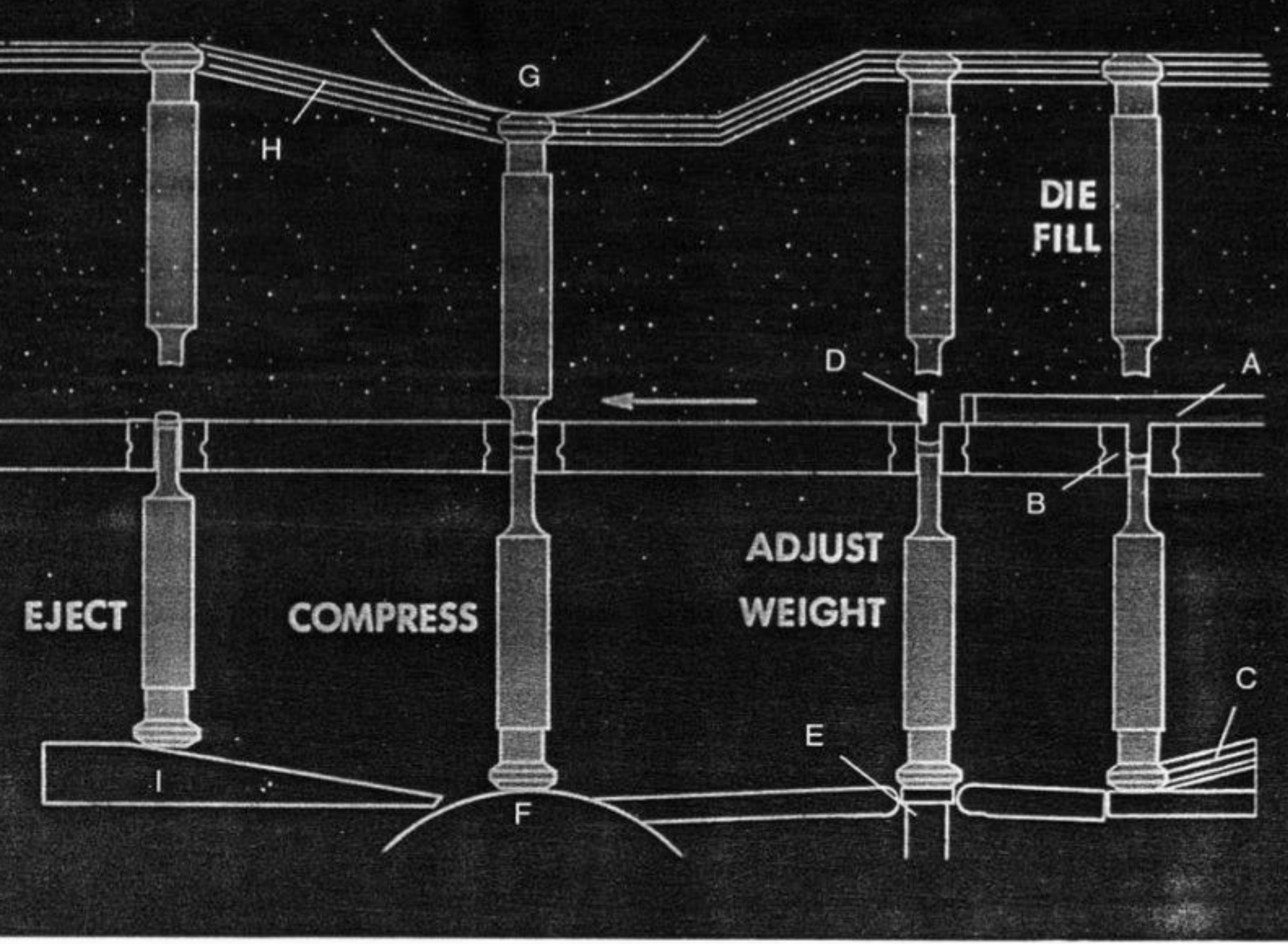
ithdrawn as they follow the **upper punch raising cam (H**

The lower punches ride up the cam (I) which brings the tab

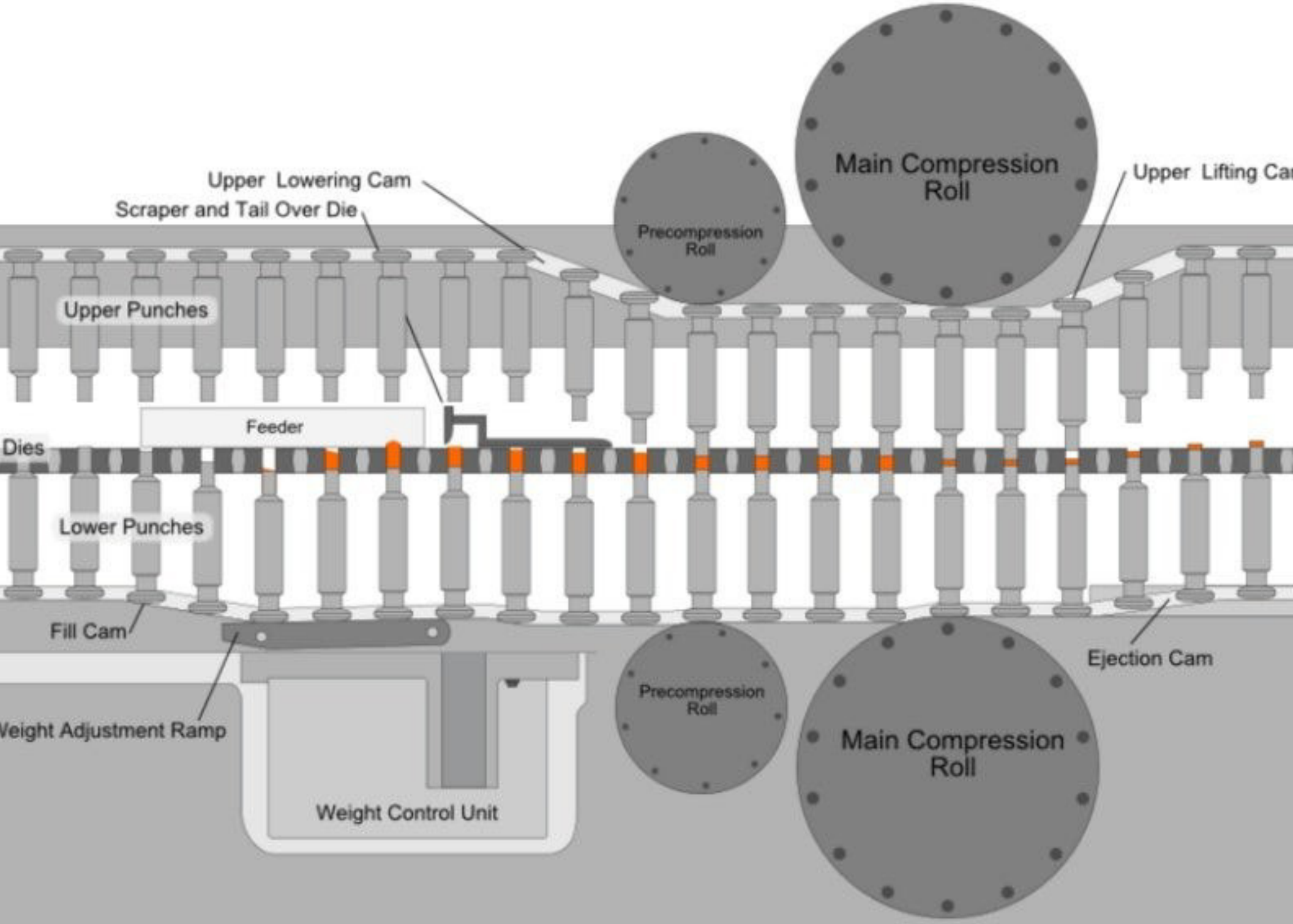
lush with or slightly above the surface of the dies

The tablets strike a sweep off blade affixed to the front of t
eed frame (A) and slide down into a receptacle

At the same time, the lower punches re-enter the pull down
am (C) and the cycle is repeated



11-6. *The compression cycle of a rotary tablet press. (See text for explanation of lettered labels.) (Courtesy of Th*


Upper Lowering Cam
Scraper and Tail Over Die
Precompression Roll
Main Compression Roll
Upper Lifting Cam
Upper Punches
Feeder
Dies
Lower Punches
Fill Cam
Ejection Cam
Weight Adjustment Ramp
Precompression Roll
Main Compression Roll
Weight Control Unit

umerous mechanical modifications over the years, the
ompaction of materials between a pair of moving punches
vithin a stationary die has **remained unchanged**

The principle modification from earlier equipment has been
ncrease in production rate which is regulated by

- ✓ Number of tooling sets
- ✓ Number of compression stations
- ✓ Rotational speed of the press

Special adaptations of tablet machines allow for the compression of layered tablets and coated tablets

A device that chills the compression components to allow the compression of low-melting point substances such as waxes i.e. suppositories

Compression Machine Tooling

PUNCHES

- **BB Tooling**:
  5.25" L, BD 0.75", 1".
- **B Tooling**: LP 3 9/16"
- **D Tooling**: Large tablets
  L 5.25", BD 1", 1 ¼" HD.

DIES

OD 0.945" 7/16" RT or 9/16" Cap T

OD 1 3/16" – 9/16" RT, 3/3" Cap T

Evaluation of Tablet

eneral Appearance:

The general appearance of a tablet, its identity and general elegan
tial for consumer acceptance, for control of lot-to-lot uniformity and ta
blet uniformity. The control of general appearance involves
urement of size, shape, color, presence or absence of odor, taste etc.

ze & Shape:

t can be dimensionally described & controlled. The thickness of a tabl
variables. Tablet thickness can be measured by micrometer or by o
e. Tablet thickness should be controlled within a ± 5% variation of stan

. Unique identification marking:

These marking utilize some form of embossing, engraving or printin
These markings include company name or symbol, product cod
product name etc.

. Organoleptic properties:

Color distribution must be uniform with no mottling. For visual colo
comparison compare the color of sample against standard color.

. Hardness :

Tablet requires a certain amount of strength or hardness and resistanc
to friability to withstand mechanical shocks of handling i
manufacture, packaging and shipping. Hardness generally measure

Different Hardness Tester

Monsanto

Pfizer

Strong-c

Friability:

bility of a tablet can determine in laboratory by Roche friabilator. T
sist of a plastic chamber that revolves at 25 rpm, dropping the tab
ugh a Distance of six inches in the friabilator, which is then operate
revolutions. The tablets are reweighed. Compress tablet that lose less th
o 1.0 % of the Tablet weigh are consider acceptable.

7. Drug Content and Release:

Weight Variation test (U.S.P.):

ake 20 tablet and weighed individually. Calculate average weight and comp
dual tablet weight to the average. The tablet pass the U.S.P. test if no more
are outside the percentage limit and if no tablet differs by more than 2 ti
tage limit.

Content Uniformity Test:

andomly select 30 tablets. 10 of these assayed individually. The Tablet pass

of the 10 tablets must contain not less than 85% and not more than 115% of th
beled drug content and the 10th tablet may not contain less than 75% and more

Disintegration Test (U.S.P.):

S.P. device to test disintegration uses 6 glass tubes that are 3" long;
and 10 mesh screen at the bottom end. To test for disintegration ti
s placed in each tube and the basket rack is positioned in a 1-L be
simulated gastric fluid or simulated intestinal fluid at 37 ± 2^0 C such
emain 2.5 cm below the surface of liquid on their upward movement
han 2.5 cm from the bottom of the beaker in their downward mo
he basket containing the tablets up and down through a distance of 5-
ency of 28 to 32 cycles per minute. Floating of the tablets can be pr
ing perforated plastic discs on each tablet.

ording to the test the tablet must disintegrate and all particles must pass thr
10 mesh screen in the time specified. If any residue remains, it must have a
s.

integration time: Uncoated tablet: 5-30 minutes

Coated tablet: 1-2 hours

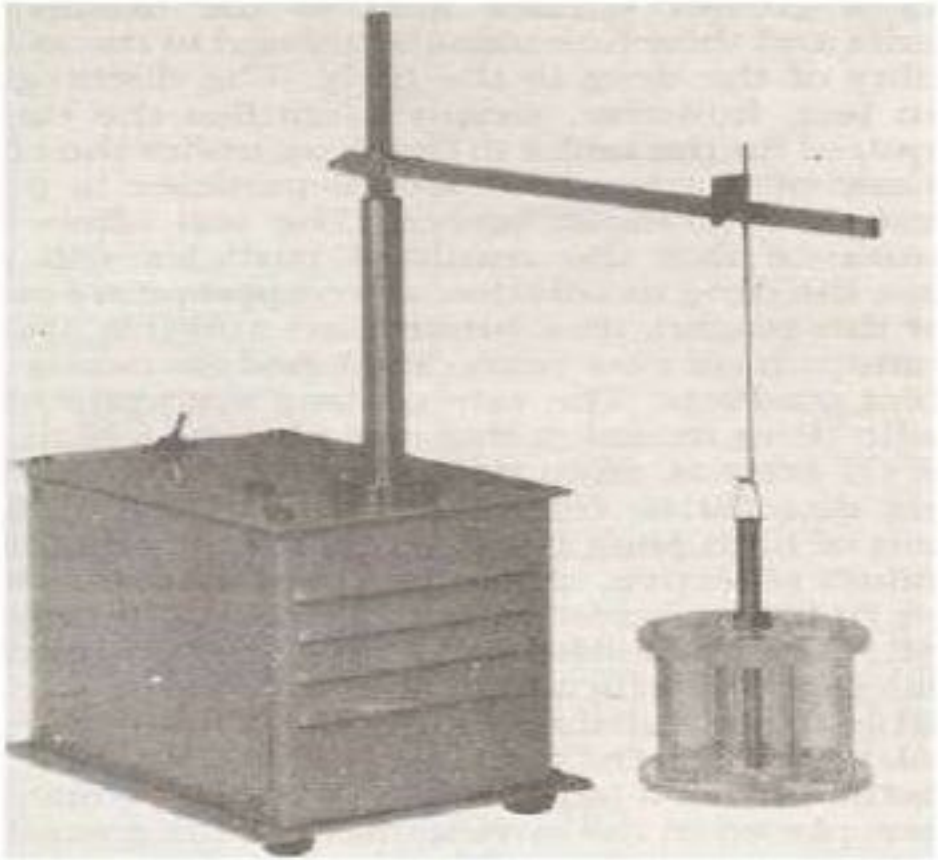


Fig. 18 Disintegration test apparatus

set of apparatus:

Apparatus-1:

gle tablet is placed in a small wire mesh basket attached to the bottom
connected to a variable speed motor. The basket is immersed in a disso
um (as specified in monograph) contained in a 100 ml flask. The fl
drical with a hemispherical bottom. The flask is maintained at 37±0.5°
tant temperature bath. The motor is adjusted to turn at the specified
sample of the fluid are withdrawn at intervals to determine the amo
in solutions.

Apparatus-2:

is same as apparatus-1, except the basket is replaced by a paddle. T

sage form is allowed to sink to the bottom of the flask before stirring. F

solution test U.S.P. specifies the dissolution test medium and volum

e of apparatus to be used, rpm of the shaft, time limit of the test a

ay procedure for. The test tolerance is expressed as a % of the label

ount of drug dissolved in the time limit.

g. 20 Dissolution test apparatus

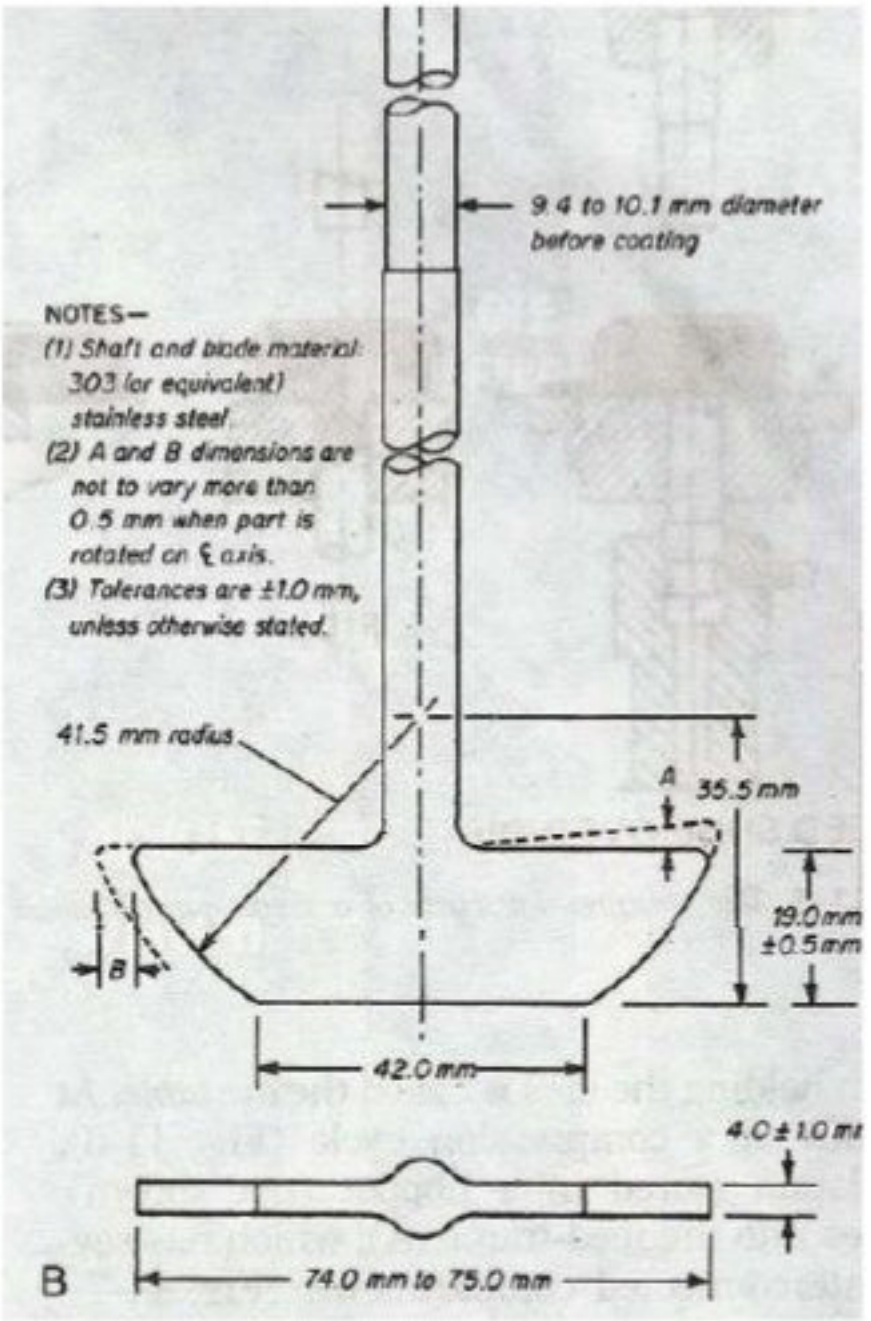


Fig. 22 USP dissolution apparatus 2

Problems In Tableting

Capping

Lamination / Laminating

Chipping

Cracking

Sticking / Filming

Picking

Binding

Mottling

Double impression

Granule Size and size distribution

Poor flow

Punch Variation

CAUSES	REMEDIES
Large amount of fines in the granulation	Remove some or all fines 100 to 200 mesh scr
Too dry or very low moisture content (leading to loss of proper binding action).	Moisten the granules suita hygroscopic substance e.g. methyl- cellulose or PE
Not thoroughly dried granules.	Dry the granules prop
Insufficient amount of binder or improper binder.	Increasing amount of bi Adding dry binder such gelatinized starch, gum powdered sorbitol, PVP, h silica or powdered su
Insufficient or improper lubricant.	Increase the amount of lu change the type of lubr
Granular mass too cold to compress firm.	Compress at room temp

o.	CAUSES	REMEDIES
	Poorly finished dies	Polish dies properly. Investigat steels or other materials.
	Deep concave punches or beveled-edge faces of punches.	Deep concave punches or bevel faces of punches.
	Lower punch remains below the face of die during ejection.	Make proper setting of lower during ejection.
	Incorrect adjustment of sweep-off blade.	Adjust sweep-off blade corre facilitate proper ejection
		Reduce speed of turret (Increas

MACHINE (Dies, Punches and Tablet Press)]

CAUSES	REMEDIES
pid relaxation of the peripheral regions of a let, on ejection from a die.	Use tapered dies,
pid decompression e pre-compression step.	Reduce turret speed and reduce compression pressure.

Causes And Remedies Of Chipping Related To Formulation (Granulation) Are As Follows

No.	CAUSES	REMEDIES
.	Sticking on punch faces	Dry the granules properly or increase lubrication.
.	Too dry granules.	Moisten the granules to plasticize. Add hygroscopic substances.

MACHINE (DIES, PUNCHES AND TABLET PRESS)

CAUSES	REMEDIES
Groove of die worn at compression point.	Polish to open end, reverse or replace the
Barreled die (center of the die wider than ends)	Polish the die to make it cylindrical
Edge of punch face turned inside/inward.	Polish the punch edges
Concavity too deep to compress properly.	Reduce concavity of punch faces. Use flat p

CAUSES AND REMEDIES OF CRACKING RELATED TO FORMULATION (GRANULATION)

CAUSES	REMEDIES
Large size of granules.	Reduce granule size. Add fines.
Too dry granules.	Moisten the granules properly ar proper amount of binder
Tablets expand.	Improve granulation. Add dry binders

MACHINE (DIES, PUNCHES AND TABLET PRESS)

CAUSES	REMEDIES
Tablet expands on ejection due to air entrapment.	Use tapered die.
Deep concavities cause cracking while	removing tablets Use special take-off

THE CAUSES AND REMEDIES OF STICKING RELATED TO FORMULATION (GRANULATION)

CAUSES	REMEDIES
Granules not dried properly.	Dry the granules properly. Make moist analysis to determine limits.
Too little or improper lubrication	Increase or change lubricant.
Too much binder	Reduce the amount of binder or use different type of binder.
Hygroscopic granular material.	Modify granulation and compress und controlled humidity.
Oily materials	Modify mixing process. Add an absorb

CAUSES	REMEDIES
Concavity too deep for granulation.	Reduce concavity to optimum.
Too little pressure.	Increase pressure.
Compressing too fast.	Reduce speed

CAUSES AND REMEDIES OF PICKING RELATED TO FORMULATION (GRANULATION)

CAUSES	REMEDIES
Excessive moisture in granules.	Dry properly the granules, determine optim limit.
Too little or improper lubrication.	Increase lubrication; use colloidal silica as 'polishing agent', so that material does not cli punch faces.
Low melting point substances, may soften from the heat of compression and lead to picking.	Add high melting-point materials. Use high m point lubricants.
Low melting point medicament in high concentration.	Refrigerate granules and the entire tablet pr
Too warm granules when compressing	Compress at room temperature. Cool sufficie

	CAUSES	REMEDIES
	Rough or scratched punch faces.	Polish faces to high luster.
	Embossing or engraving letters on punch faces such as B, A, O, R, P, Q, G.	Design lettering as large as possib Plate the punch faces with chromium to a smooth and non-adherent face
	Pressure applied is not enough; too soft tablets.	Increase pressure to optimum.

AUSES AND REMEDIES OF BINDING RELATED TO FORMULATION (GRANULA

	CAUSES	REMEDIES
	Too moist granules and extrudes around lower punch.	Dry the granules properly.
	Insufficient or improper lubricant.	Increase the amount of lubricant or use a more lubricant
	Too coarse granules.	Reduce granular size, add more fines, and incre quantity of lubricant.
	Too hard granules for the lubricant to be effective.	Modify granulation. Reduce granular size
	Granular material very abrasive and cutting into dies.	If coarse granules, reduce its size. Use wear-resis

CAUSES	REMEDIES
Poorly finished dies.	Polish the dies properly.
Rough dies due to abrasion, corrosion.	Investigate other steels or other materials or granulation.
Undersized dies. Too little clearance.	Rework to proper size. Increase clearance.
Too much pressure in the tablet press.	Reduce pressure. OR Modify granulation.

CAUSES AND REMEDIES OF MOTTLING

.	CAUSES	REMEDIES
	A coloured drug used along with colourless or white-coloured excipients.	Use appropriate colourants.
	A dye migrates to the surface of granulation while drying.	Change the solvent system, Change the binder, Reduce drying temperature and Use a smaller particle size.
	Improperly mixed dye, especially during 'Direct Compression'.	Mix properly and reduce size if it is of a larger prevent segregation.
	Improper mixing of a coloured binder solution.	Incorporate dry colour additive during powder step, then add fine powdered adhesives such as ac

Tablet Coating

ablet coating objectives.

ree Primary components involved in tablet coating

ablet properties

oating process

- Coating equipment.
- Parameters of the coating process.
- Facility and ancillary equipment.
- Automation in coating processes.

oating compositions

1. Tablet Properties

- Mechanical and Physical Strength
- Smooth surface
- Physical shape
- Chemical nature of tablet ingredients
- Hygroscopicity

Coating Process

- **Three types of equipments**
  1. The standard coating pan
  2. The perforated coating pan
  3. The fluidized bed (Air suspension) coater.

- **These systems based on three basic designs**

1. Conventional pan system

Depending on drying efficiency

- Pellegrini system
- Immersion-sword system
- Immersion –tube system

2. Perforated pan system

- Accela-coata
- Hi-coater systems
- Driacoater
- Glatt coater

3. Fluidized bed (Air suspension) system

inches diameter revolving on its horizontal axis.

ed air is directed **into** the **pan** and **onto** the **tablet bed**

e.

usted by means of **ducts** positioned through the **front of**

n

ing efficiency is achieved by,

legrini pan:

a **baffled pan** and

user for uniform distribution

rying air.

closed and **automated**.

ng air through perforated

sword immersed in the

ped.

ard flow through bed.

ay onto the bed surface

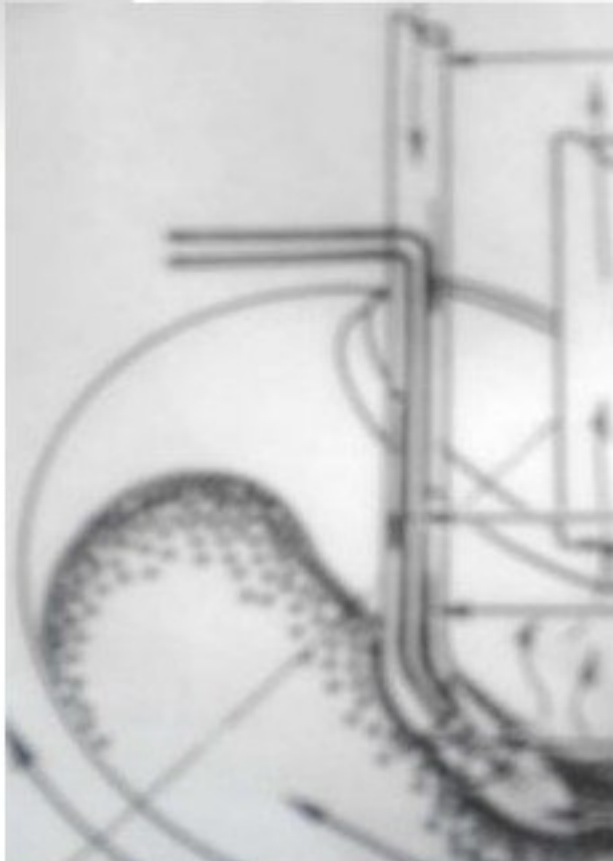
ersion-tube system

immersed in tablet bed

ers heated air and coating solution through

y built in the tip of tube

s upward and exhausted by a conventional duct.



ated drum rotates on its horizontal axis in an

ed housing.

a-Coata and **Hi-coater system**: **Drying air** is

ed **in to drum**, is **passed** through **bed**, and is

sted through **perforations** in to drum.

Eight Gun Manifold Spray Bar
Titanium or stainless steel construction available.

oater:

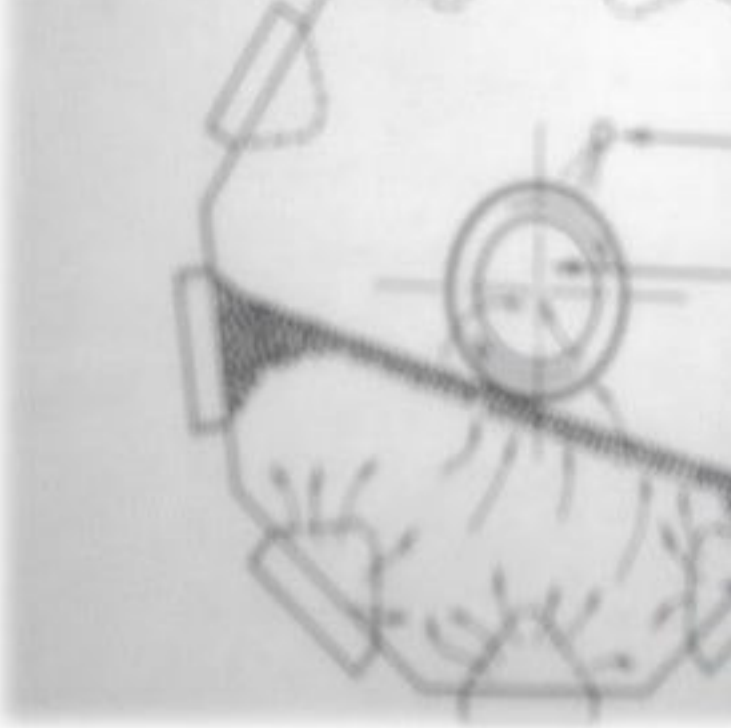
oduces **drying air** through hollow **perforated**

s located inside periphery of the drum.

h rotating pan, **ribs dip into bed**

ing air **passes up** through and **fluidizes bed**

haust is from **back** of the **pan**



coater:

ing air directed **from inside** the drum

ugh **bed** and out an **exhaust duct**

an optional split-chambered plenum

ng air can be directed in the **reverse** manner

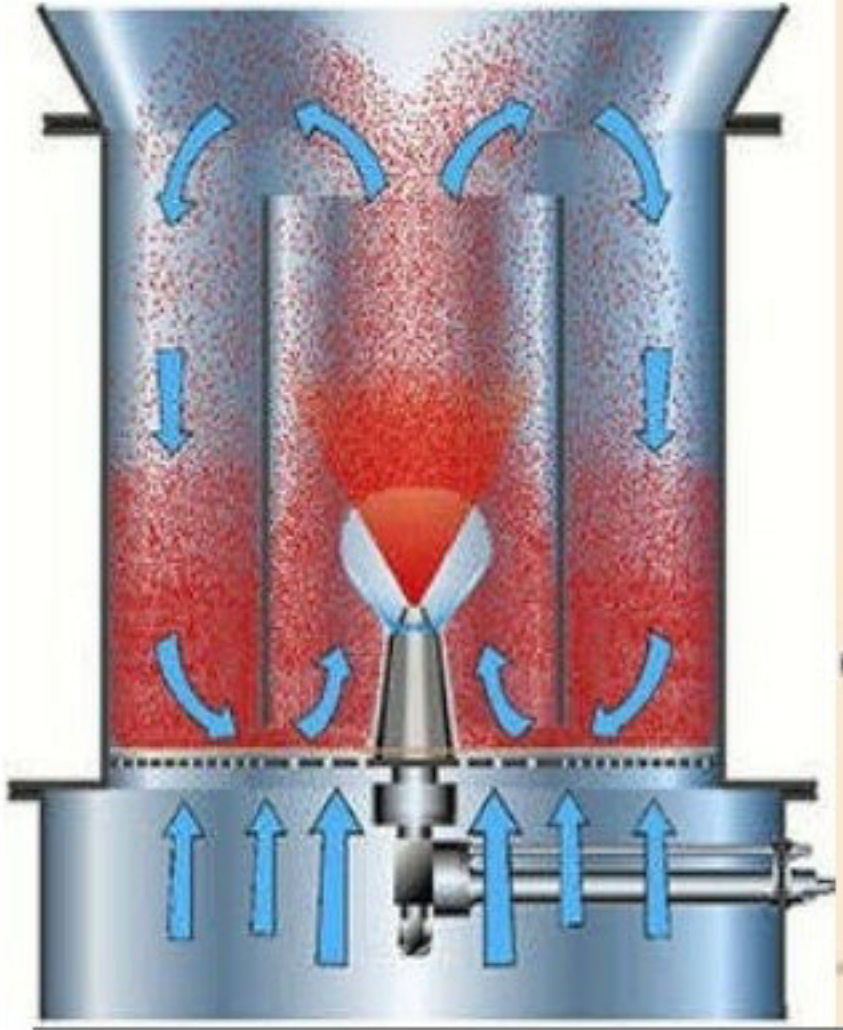
eral air flow configurations are possible.

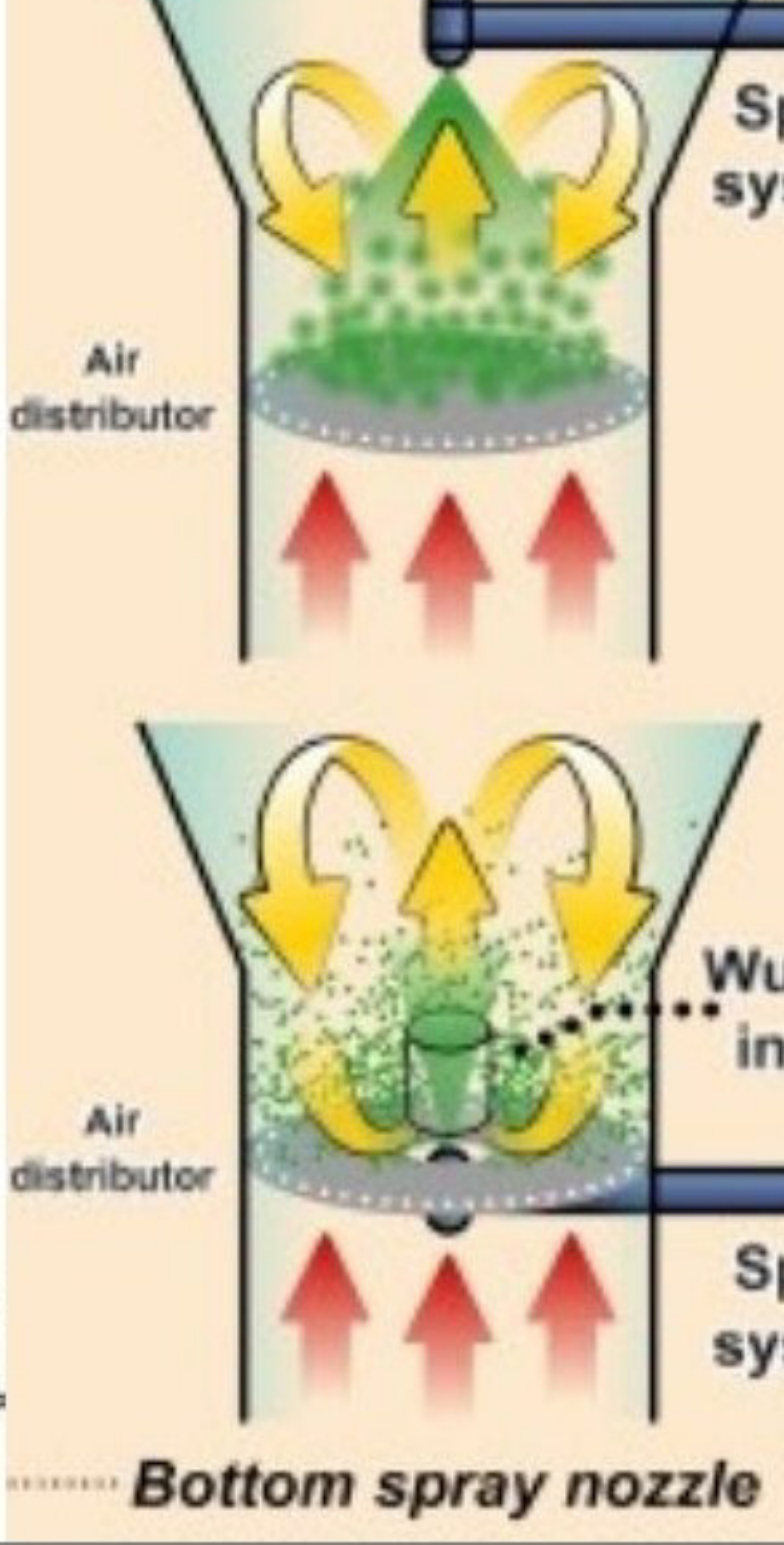
hly efficient

idization of tablet bed is achieved in a

umnar chamber by the upward flow of

ing air.





Spray application System

asic **types** of **spray system** differ in manner in which **atomization** of l

eved

h-pressure, airless (a)

High pressure liquid (250-3000psig) through a small orifice (.009"- .0

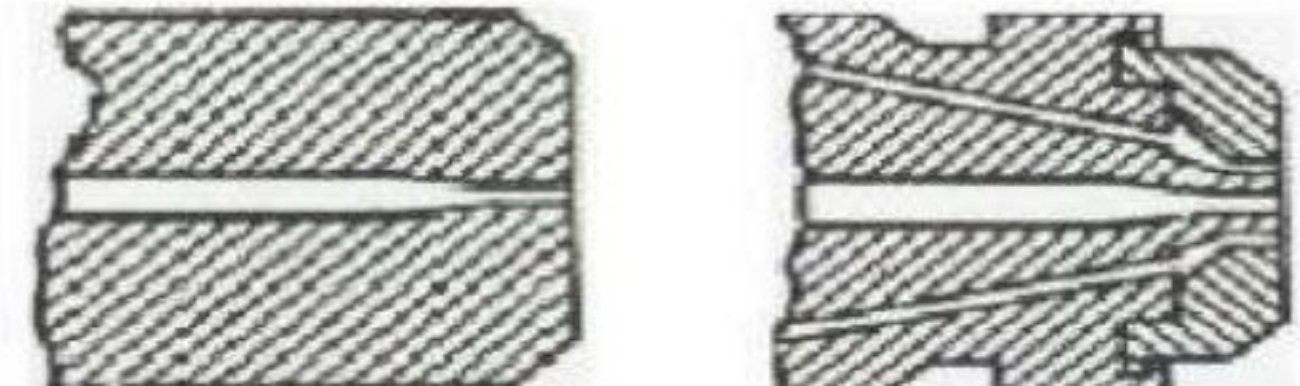
Degree of automization- fluid pressure, orifice size, viscosity.

***w*-pressure, air-automized (b)**

Low pressure liquid (5-50psig) through a large orifice (.020"- .060" id)

Degree of automization- fluid pressure, orifice size, viscosity, air pres

air cap design.



Parameters of Coating Process

e of coating composition application= Rate of evaporation of volatile s

viation from this results a serious coating problems

Mathematical modeling for automated aqueous coating pro

$$A(T_1,H_1)+C_1(S)+pSA_1 \xrightarrow{E} A(T_2,H_2)+C_2+pSA_2 \quad \textit{Exhau}$$

re,

H) = Air capacity, C(S) = Coating Compositi

SA = Tablet surface area, E = Equipment efficien

pacity:

antity of water or solvent removed during coating process

pends on : 1. Quantity of air flow through tablet bed,

2. Temperature of air,

3. water content of inlet air.

g Composition:

t air-heated, exhaust air- cool.

ing of film- rate of application

n rapidly drying formulations dry quickly on the tablet surface allowing

stant application by efficient atomization of coating solution

e and presence of debossed features affects coating conditions

al surface area per unit weight decreases from smaller to larger tablet

same thickness of film, smaller tablets requires more coating composi

npared with larger tablets

e of atomized coating droplets must be smaller and better controlled as

tures to be coated become smaller.

ment efficiency, E:

$$\text{g Efficiency, E} = \frac{\text{Net increase in coated tablet weight}}{\text{Total nonvolatile coating weight applied to tablets}}$$

Facility and Ancillary Equipment

y should meet to requirement of cGMP

ıate space for equipment, processing, in-process storage

requirements depending on nature of solvent- electrical explosion-pro

ılized ventilation

st air treatment to recover solvent or to prevent entry in to atmosphere

al EPA defines limits of organic solvents and particulate allowed in atm

ous based coating is advantageous

Equipments

ters, mixers, mills, jacketed tanks, portable pressure tanks or pumping

Tablet Coating Process

Final production step on which quality of product may be judged

Sugar Coating

involves,

1. Sealing,
2. Subcoating
3. Syruping (Smooting)
4. Finishing
5. Polishing

prevent moisture penetration into tablet core

ecially in pan-ladling process in which localized overwetting of portion c

let bed occur

llac

fects disintegration and dissolution time due to polymerization on aging

n

ch effect is not reported

coating

round the edges and build up size .

coating Steps

binder solution → Dusting of subcoating powders → Dryin

cover and fill in the imperfections in tablet surface caused by subcoatin

impart desired color

st syrup coat contains some suspended powders i.e. grossing syrups

ute colorants– tinted base– uniform coating

rup solution containing dye applied until final size and color are achieve

ishing

al syrup coating step

w clear coats of syrup may be applied

ishing

sired luster is obtained in this final step

ean standard coating pan, canvas-lined coating pans

oating are given below:

ating	Sub coating	Syrup coating	Polishing sol
nellac	Gelatin	Colorant	Carnauba wa
cid	Acacia	Sub coating powder	(yellow)
ene glycol	Sugar cane powder	Cal. Carbonate	Bees wax
000	Corn syrup	Cane sugar powder	(white)
ene chloride	Syrup	Corn starch	Paraffin wax
l	Distilled water	Syrup	Naphtha
		Distilled water	

c coating polymers: Cellulose acetate phthalate, Acrylate poly
xypropyl methyl cellulose phthalate, Polyvinyl acetate phthalate

ts used for coating: Ethanol, Methanol, Isopropanol, Chloroform, Aceto
ene chloride, Methylene ethyl ketone

Film Coating

n coating and sugar coating shares the same equipments and process

ameters

o methods,

1) Pan-Pour method

as that of pan-pour sugar coating

d is relatively slow and relies heavily on skill and technique of operator

us based film coating is not suitable due to localized over-wetting

2) Pan-Spray method

f automated spraying system

Process Variables

ensure the consistent product quality, certain elements of process need to be
ntrolled regardless of coating pan system

e variables to be controlled in pan-spray film coating process are:

n variables

- Pan design/ baffling
- Speed
- Pan load

ocess air

- Air quality
- Temperature
- Airflow rate/ volume/ balance

ray variables

- Spray rate
- Degree of atomization
- Spray pattern

er vapor permeability

tensile strength

ted Tablet Evaluation

Adhesion test with tensile strength tester

Diametral crushing strength of coated tablets Rate of coated tablet

disintegration/ dissolution

Stability studies

Surface roughness, hardness, color uniformity through instrumental me

Visual inspection for coated tablet quality.

Qualitative measure of resistance of a coated tablet to abrasion by whi

Coating Formula Optimization

odifications in basic formula,

- To improve adhesion of the coating to the core
- To decrease bridging of intagliations
- To increase coating hardness
- To improve any other property as per need of formulation

mmon modifications are

- Changes in polymers-to-plastisizers ratio
- Addition of different polymers or plstisizers

d have following attributes;

ubility in solvent

ubility required for intended use

pacity to produce elegant looking product

bility with heat, light, moisture, air, substrate. Essentially no color, taste

mpatibility with common coating solution additives

ntoxic , therapeutically inert and ease of application to the particles or t

sistance to cracking, and provision of adequate moisture, light, odor, or

olimation barrier when desired

bridging or filling of the debossed tablet surfaces by the film former

ilm Formers

fied in ***Nonenteric*** and ***Enteric*** Materials

nenteric Materials

- HPMC,
- MHEC,
- EC,
- HPC,
- Povidone,
- SCMC,
- PEG,
- Acrylate Polymers

asons for enteric coating

tect acid labile drugs from gastric fluid e.g. enzymes, ATBTs

vent gastric distress or nausea due to irritation from drug, e.g. Sodium

deliver drugs for local action in intestines, e.g. Intestinal antiseptic (Kar

drugs optimally absorbed in small intestine

vide delayed release component for repeat-action tablets

terial should have following properties

- Resistance to gastric fluids
- Ready susceptibility or permeability to intestinal fluids
- Stability with coating composition and drug substrate
- Stability alone and in coating solution
- Formation of continuous film
- Nontoxicity, Low cost

CAP,

Acrylate Polymers

HPMCP

PVAP

Solvents

Plasticizers

nal" or "External" techniques

Colorants

Opaquant-Extenders

Miscellaneous Coating Solution Components

- Quality Control
- Stability Testing
- Film Defects
- Specialized Coatings
  - Compression Coating
  - Electrostatic Coating
  - Dip Coating
  - Vacuum Film Coating

oblems And Remedies for Tablet Coa

- Blistering
- Chipping
- Cratering
- Picking
- Pitting
- Blooming
- Blushing
- Colour variation
- Infilling
- Orange peel/Roughness

	CAUSES	REMEDIES
	Effect of temperature on the strength, elasticity and adhesion of the film	Use mild drying condition.
	THE CAUSE AND REMEDY OF CHIPPING	
	High degree of attrition associated with the coating process.	Increase hardness of the film by increasing the m weight grade of polymer.
	THE CAUSES AND REMEDIES OF CRATERING	
	Inefficient drying.	Use efficient and optimum drying conditio
	Higher rate of application of coating solution.	Increase viscosity of coating solution to decreas application rate.
	THE CAUSES AND REMEDIES OF PICKING	
	Inefficient drying.	Use optimum and efficient drying conditions or in inlet air temperature.
	Higher rate of application of coating solution	Decrease the rater of application of coating sol increasing viscosity of coating solution.
	THE CAUSE AND REMEDY OF PITTING	
	Inappropriate drying (inlet air) temperature	Dispensing with preheating procedures at the ini coating and modifying the drying (inlet air) tempe that the temperature of the tablet core is not great melting point of the batch of additives use
	THE CAUSE AND REMEDY OF BLOOMING	

High coating temperature	Decrease the drying air temperatu
Use of sorbitol in formulation which causes largest fall in the thermal gelation temperature of the Hydroxy Propyl Cellulose, Hydroxy Propyl Methyl Cellulose, Methyl Cellulose and Cellulose ethers.	Avoid use of sorbitol with Hydroxy Propyl Cellu Propyl Methyl Cellulose, Methyl Cellulose an ethers.

THE CAUSE AND REMEDY OF COLOUR VARIATION

Improper mixing, uneven spray pattern, insufficient coating, migration of soluble dyes-plasticizers and other additives during drying.	Go for geometric mixing, reformulation with plasticizers and additives or use mild drying

THE CAUSE AND REMEDY OF INFILLING

Bubble or foam formation because of air spraying of a polymer solution	Add alcohol or use spray nozzle capable atomization.

THE CAUSES AND REMEDIES OF ORANGE PEEL/ROUGHNESS

Rapid Drying	Use mild drying conditions
High solution viscosity	Use additional solvents to decrease viscosity

THE CAUSE AND REMEDY OF CRACKING/SPLITTING


Thank You
If you salute your duties, No need to salute anybody
If you don't salute your duties, You have to salute everybody.