Course Code: BPHT3004 Course Name: Pharmaceutical Engineering

TOPIC: MIXING

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Mixing may be defined as a unit operation that aims to treat two or more components, initially in an unmixed or partially mixed state, so that each unit (particle, molecule etc.) of the components lies as nearly as possible in contact with a unit of each of the other components.

Application of mixing:

- •Mixing is an intermediate stage in the preparation of several dosage forms.
- •Wet mixing in the granulation step in the production of tablet
- •For dilution of potent active drugs

Types of mixtures

Positive mixtures - Positive mixtures are formed from materials such as gases or miscible liquids which mix spontaneously and irreversibly by diffusion, and tend to approach a perfect mix.•

Negative mixtures- With negative mixtures the components will tend to separate out. If this occurs quickly, then energy must be continuously input to keep the components adequately dispersed, e.g. with a suspension formulation, such as calamine lotion.

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Neutral mixtures - Neutral mixtures are said to be static in behavior, i.e. the components have no tendency to mix spontaneously or segregate spontaneously once work has been input to mix them. Examples of this type of mixture include mixed powders, pastes and ointments.

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FACTORS AFFECTING MIXING

- 1. Mechanism of mixing
- 2. Density of the particles
- 3. Particle size
- 4. Particle shape
- 5. Particle charge

Types of mixing

Solid-solid mixing

- 2. Liquid-liquid mixing
- 3. Mixing of immiscible liquids
- 4. Solid-liquid mixing

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Solid-solid mixing:

This is the process in which two or more than two solid substance are mixed in a mixer by continuous movement of the particle.

Mechanism of mixing in solids:

1- convective mixing (macro mixing)

Material in the mixer is transported from one location to another.

This type of mixing process will lead to a less ordered state inside the mixer

The components which have to be mixed will be distributed over the other components

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Usually this type of mixing is applied for free-flowing and coarse materials

> Shear mixing:

Force of attraction are broken down so that each particles moves on its own between region of different composition.

> Diffusive mixing (micro mixing):

Random motion of particles within the powder bed thereby particle change their position relative to one another.

Solid-solid mixing steps

In the solid-solid mixing operation four steps are involved:

- 1. Expansion of the bed of solid
- 2. Application of three dimensional shear forces to the powder bed
- 3. Mix long enough to permit true randomization of particle
- 4. no segregation after mixing

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Methods of solid-solid mixing

The powders may be mixed by following methods:

- 1. Spatulation
- 2. Trituration
- 3. Tumbling
- 4. Geometric dilution

Classification of mixers:

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) Batch Type mixers

- 1. Tumblers
- 2. V-cone blender or twin shell blender
- 3. Double cone blender
- 4. Tumbling blender with agitator mixing blade
- 5. Ribbon blender
- 6. Sigma blade mixer
- 7. Planetary mixer
- 8. Fluidized mixer

b) Continuous Type mixers

- 1. Barrel type continuous mixer
- 2. Zigzag type

Based on flow properties

Free flowing solids

- •V cone blender
- Double cone blender

2. Cohesive solids

Sigma blender

Planetary blender

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With out meixing hotage

With mixing blade

Capacities: smaller models 20kg rotate at 35rpm

Larger model 1 tonne 15rpm

Advantages: easy to clean & maintain

Handle large capacities

Disadvantages: not suitable for very fine and particles with greater particle size difference

due to less shear

Double cone blender

30-100rpm.

Mixing occurs due to tumbling.

For homogenous mixing of powders and granules

Jacketed construction for heating and cooling

Advantages: easy to clean & maintain

Handle large capacities

Disadvantages: not suitable for very fine and particles with greater particle size difference

due to less shear

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Ribbon blender

Principle:

Mechanism of mixing is shear. Shear is transferred by moving blades. High shear rates are effective in breaking lumps and aggregates. Convective mixing also occurs as the powder bed is lifted and allowed to cascade to the bottom of the container

Construction:

- Blades have both right and left hand twists.
- Blades are connected to fixed speed drive.
- It can be loaded by top loading and emptying is done through bottom port.

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For mixing finely divided solids, wet solid mass, sticky & plastic solids.. It is used for liquid-solid & solid-solid mixing

Advantages: High shear can be applied by using baffles, which bring about a rubbing & break down aggregates. **Disadvantages**: Shearing action is less than in planetary mixer.

Sigma blade mixer

Construction and working:

- Two sigma shaped blades are fitted horizontally in the bowl.
- These blades are connected to a fixed speed drive.
- Mixer is loaded from top and unloaded by tilting the entire bowl.
- The blades move at different speeds, one about twice than the other, which allows movement of powder from sides to centers.
- The material also moves top to downwards and gets sheared between the blades and the wall of the tough resulting cascading action.
- Perforated blades can be used to break lumps and aggregates which creates high shear forces.

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Planetary mixer:

it works on the principle of shearing & convective in action.

Single planetary mixer: for light, medium viscosity products in the pharmaceutical, cosmetic & food industry.

Double planetary mixer: in chemicals, rubber & other allied industries.

Jacketed construction available for heating & cooling.

Applications. Advantages speed of rotation can be varied so it is **advantageous** over sigma blade or ribbon type blender. Disadvantages It requires high power. It has limited size & is useful for batch work only.

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Liquid-liquid mixing: Liquid-liquid mixing is the formation Of homogenous system by the application of shear. The mechanism of mixing can be classified into four classes.

- 1. Bulk transport
- 2. Turbulent
- 3. Laminar mixing
- 4. Molecular diffusion

Mixing equipments for liquid-liquid mixing

The mixing apparatus consist a container (tank) and a mixing device. A mixing device is called impeller, which is mounted with the help of shaft. The shaft is driven by a motor. Three main types of impeller are used namely-

- 1. Propeller
- 2. Turbine
- 3. Paddles

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Propeller

- •Run at 8000rpm
- Provides longitudinal movement of liquid
- •It is used for low viscosity liquids

Disadvantage: little shear so not suitalbe for emulsification

Turbine

- •4, 6 or 8 blades...(axial turbine or radial turbine)
- Diameter is 30-50% of vessel
- •Rotates at lower speed 50-200rpm

More shear force suitable for viscous liquids

Paddles:

- •2 or 4 blade paddles are common
- •They have large surface area
- •Rotate at 100rpm
- •Useful for viscous and semisolid preparations

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Mixing of immiscible Liquids

Carried mainly in the manufacture of emulsions, and the equipment used for the preparation of an emulsion is known as emulsifier. Also known as homogenizer as it results in fine emulsion.

Fine emulsion is prepared in 2 stages.

1st stage coarse emulsion is prepared by using one of the :-

Wedge wood

Mechanical blender

Hand homogenizer

Porcelain mortar and pestl.

2nd stage

Silverson emulsifier

Colloidal mill

Rapisonic homogenizer

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Silverson mixer –Emulsifier

Principle:

It produces intense shearing forces and turbulence by use of high speed rotors Circulation of the material ensures rapid breakdown of the dispersed liquid into smaller globules Blades are surrounded by a mesh,

Uses:

Used for the preparation of emulsions and creams of fine particle size.

Advantages:

- Silver son mixer is available in different sizes to handle the liquids ranging from a few millI liters to several thousand liters.
- •Can be used for batch operations as well as for continuous operations by incorporating into a pipeline, through which the immiscible liquids flow.

Disadvantages:

Occasionally, there is a chance is clogging of pores of the mesh

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