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Mixing Part 2	عنوان المحاضرة باللغة الانجليزية
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The Theory and Practice of Industrial Pharmacy By Leon Lachman et al.	المصادر والمراجع

محتوى المحاضرة

Kneaders

Sigma-Blade Mixer

Sigma-blade mixer has counter-rotating blades or heavy arms that work the plastic mass. The blades rotate tangentially with a speed ratio of about 2:1. The shape and difference in rotational speed of the blades facilitate lateral pulling of the material and impart kneading and rolling action on the material

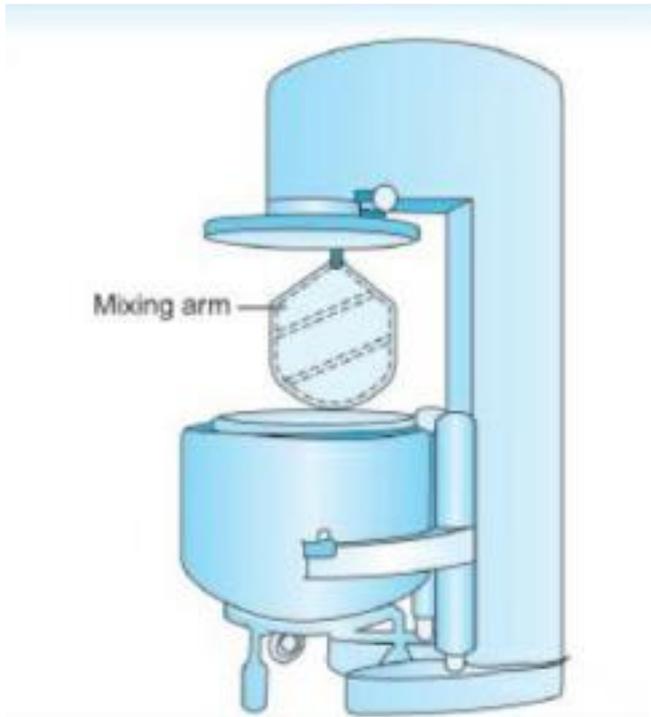
.Shear forces are also generated by the high viscosity of the mass and are thus effective in deaggregation as well as distribution of solids in the

fluid vehicle.

Planetary Mixer

It imparts planetary mixing action, whereby the mixing element

rotates round the circumference of the mixer's container, while simultaneously rotating about its own axis. The double rotation of the mixing element and its offset position reduces the dead zones and avoids vortex formation.



Mulling Mixers

Mulling mixers provide forces that incorporate kneading, shearing, smearing, and blending of materials for a total uniform consistency. This process produces just enough pressure to move, intermingle and push particles into place without crushing, grinding, or distorting the ingredients. The result is a final mixture of truly uniform consistency in both physical and chemical structure.

Mulling

Mixers are efficient in deaggregation of solids, but are typically inefficient in distributing the particles uniformly throughout the entire mass. These devices are suitable for mixing previously mixed material of uniform composition, but containing aggregates of solid particles. In the event of segregation during mulling, a final remixing may be necessary.

Schematic representation of the mulling mixer

Roller Mills

Roller mills consist of one or more rollers and are commonly used. Of these, the three-roller types are preferred (Fig. 1.15). In operation, rollers composed of a hard, abrasion-resistant material, and arranged to come into close proximity to each other are rotated at different rates. Depending on the gap, the material that comes between the rollers is crushed, and also sheared by the difference in rates of movement of the two surfaces.

In extreme cases of solid-liquid mixing, a small volume of liquid is to be mixed with a large quantity of solids. This process is essentially one of coating the solid particles with liquid and subsequent transfer of liquid from one particle to another. In this type of mixing, the liquid is added slowly to reduce the tendency of the particles to form a lump. However, the process is not for fluids mixing, but for solids mixing. When the particles tend to stick together because of the surface tension of the coating liquid, the equipment used is the same as that for pastes. If the solids remain essentially free flowing, the equipment is the same as that used for solids mixing.

Mixer Selection

One of the first and often most important considerations in any mixing problem is equipment selection

Factors that must be taken into consideration for appropriate mixer selection include :

(1) the physical properties of the materials to be mixed, such as density, viscosity, and miscibility,

(2) economic considerations regarding processing, for example, the time required for mixing and power expenditure necessary

(3) cost and maintenance of the equipment

however, the selection of equipment depends primarily upon the viscosity of the liquids, and is made according to the mechanism by which intense shearing forces can best be generated.

Low Viscosity Systems

Monophasic systems of low viscosity are classified as positive mixtures, and if given time, mix completely without external agitation. Agitation reduces the time required for mixing, allowing a fast decay in the intensity of segregation. In general, for low viscosity liquids no great problems are encountered unless the operational scale is very large. The viscous character and density of the fluid(s) to be mixed determine, to a large extent, the type of flow that can be produced, and therefore, also the nature of the mixing mechanisms involved. Fluids of relatively low viscosity are best mixed by methods that generate a high degree of turbulence, and at the same time circulate the entire mass of material. These requirements are satisfied by air jets, fluid jets, and the high-speed propellers discussed earlier. A viscosity of approximately 10 poises may be considered as a practical upper limit for the application of these devices.

Intermediate Viscosity Systems

The mixing of systems composed of immiscible liquids (emulsions) or finely divided solids with a liquid of low viscosity (suspensions) depends on the subdivision or deaggregation of one or more of these phases, with subsequent dispersal throughout the mass of the material to be mixed. These processes are often carried out in a single mixing operation, provided that shear forces of sufficient intensity to disrupt aggregates can be generated. At low solid-disperse phase concentrations the flow properties are Newtonian and mixing by propellers is satisfactory as long as the dispersed components oppose settling.

Under such conditions it may be desirable to increase the impeller size and decrease its speed. Emulsions and suspensions are of such viscosity that it is difficult, if not impossible to generate turbulence within their bulk, and laminar mixing, and molecular diffusion must be relied upon. Mixing of such fluids may be accomplished with a turbine of flat blade design. A characteristic feature of such impellers is the relative insensitivity of their power consumption to the density and/or viscosity of the material.

High viscosity Systems

Viscous ointments are efficiently mixed by the shearing action of

two surfaces in close proximity, and moving at different velocities with respect to each other. This is achieved in paddle mixers, in which the blades clear the container walls by a small tolerance. Such mixers are relatively efficient, since they not only generate sufficient shear to reduce globule size, but if properly constructed, also induce sufficient circulation of the material to ensure a uniform dispersion throughout the complete mixture.

As the percentage of solids is increased, or if highly viscous fluids are employed, the solid liquid system takes on the consistency of a paste or dough. For thicker pastes and plastic masses, a kneading, stretching and folding action is employed. The forces required to induce shear are considerable, and the equipment used is of heavy design. In such cases, sigma-blade mixer and muller mixer are the commonly used mixers.

Mixing of solids

- In the manufacture of tablets or granules normally a number of additives are added. Therefore, mixing of powder becomes essential part of the process.
- Mixing is considered as a critical factor, especially in case of potent drugs and low dose drugs where high amounts of adjuvants are added.
- The diverse characteristics of particles such as size, shape, volume, surface area, density, porosity, and flow charge contribute to the solid mixing.

From the definition of mixing, the ideal situation or “perfect mix” in this case would be produced when each particle lies as closely as possible in contact with a particle of the other component. Although a perfect mixture would offer a point uniformity, such arrangement is virtually impossible to get in practice by any mixing equipment.

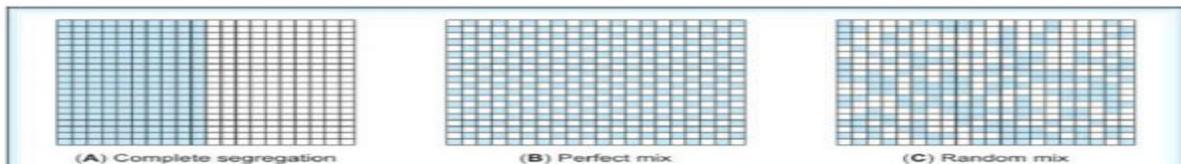
Powder mixing, however, is a “chance” process and in practice the best type of mix likely to be obtained is a “random mix” where the probability of finding one type of particle at any point in the mixture is equal to its proportion in the mixture.

Segregation is the central problem associated with the mixing and handling of the solid particles, such segregation of particulate solids can occur during mixing as well following the mixing operation

Solids tend to segregate by virtue of differences in the size,

density, shape, and other properties of the particles of which they are composed.

The second requirement for segregation can be met by the Earth's gravitational field, or by a centrifugal, electrical, magnetic field generated in the course of processing



Factors Affecting Demixing

1) Particle Size and Size Distribution

a difference in the particle sizes of components of a formulations the main cause of segregation in powder mixes. Smaller particles tend to fall through the voids between larger particles, and thus move to the bottom of the mass

Segregation problem due to particle size difference can be reduced by:

- a) Selection of a particular sized fractions (e.g. by sieving to remove fines or lumps) to achieve drug and excipients of the same narrow particle size range.
- b) Milling of components to either reduce the particle size range or to ensure all that particles are below approximately 30 μm , at which size segregation does not tend to cause serious problems
- c) Granulation of the powder mix (size enlargement) so that large numbers of different particles are evenly distributed in each segregating unit/granule.

Factors Affecting Demixing

2) Particle shape

Particle shape is important because as the shape of a particle deviates more significantly from a spherical form, the free movement it experiences along its major axis also decreases.

Spherical particles exhibit the greatest flowability, and are therefore more easily mixed, but they also segregate more easily than non-spherical particles. Irregular or needle-shaped particles may become interlocked, decreasing the tendency to segregate once mixing has occurred

Controlled crystallization during production of the drug/excipients to give components of a particular crystal shape or size range reduces the tendency to segregate.

3) Particle Charge

The mixing of particles whose surfaces are non-conducting (electrically) often results in the generation of surface charges, as evidenced by a tendency of the powder to clump following a period of agitation. Surface charging of particles during mixing is undesirable, for it tends to decrease the process of inter particulate "diffusion."

Mechanism of mixing of solids

1. Convective mixing/Macro mixing:

- Inversion of the powder bed using blades or paddles or screw element, in which large mass of material moves from one place to another.

• 2. Shear mixing:

- In this type, forces of attraction are broken down so that each particle moves on its own between regions of different components and parallel to their surface.

• 3. Diffusion mixing/Micro mixing:

- Involves the random motion of particle within the powder bed, thereby particles change their position relative to one another.

Equipments/Batch Tumblers/Blenders

A tumbling mixer consists of a container of the one of several geometric forms, which is mounted so that it can be rotated about an axis to cause movement of the material in all planes, which is necessary for rapid overall mixing.

The resulting tumbling motion is accentuated by means of baffles, lifter blades or simply by virtue of the shape of the

container

Various types of tumblers with different geometric shapes such as twin-shell, double-cone, drum, cube and tetrahedral blenders are commercially available, which may be rotated about almost any axis depending on the manufacturer.

The popular twin-shell blender is of this type and takes the form of a cylinder that has been cut in half at approximately a 45-degree angle with its long axis, and then rejoined to form a "V" shape. This is rotated so that the material is alternately collected at the bottom of the "V" and then split into two portions when the "V" is inverted. This is quite effective because the bulk transport and shear, which occur in tumbling mixers, generally, are accentuated by this design

The efficiency of tumbling mixers is highly dependent on the speed of rotation. Rotation that is too slow neither produces the desired intense tumbling or cascading motion, nor does it generate rapid shear rates.

On the other hand, rotation that is too rapid tends to produce centrifugal force sufficient to hold the powder to the sides of the mixer, and thereby, reduces efficiency

Agitator Mixers

Agitator mixers employ a stationary container to hold the material and bring about mixing by means of moving screws, paddles, or blades. Since these mixers do not depend entirely on gravity as do the tumblers, they are useful in mixing solids that have been wetted, and are

therefore in a sticky or plastic state. The high shear forces that are set up are effective in breaking up lumps or aggregates. Well-known mixers of this type include the following: **Ribbon Mixer/Blender**

It consists of a horizontal cylindrical tank usually opening at the top and fitted with helical blades or ribbons. The blades are mounted on the horizontal axle by struts, and are rotated to circulate the material to be mixed.

The helical blades are wound (in most cases) in the opposite directions to provide for the movement of material in both directions along the axis of the tank. Although little axial mixing in the vicinity of the shaft occurs, mixtures with high homogeneity can be produced by prolonged mixing even when the components differ in particle size, shape, or density, or there is some tendency to aggregate.

Continuous Mixers

A characteristic of solids mixing equipment is that all else being equal, mixtures produced by large mixers have greater variations in composition than those produced by small mixers. This is an important consideration when relatively small portions of the mixture are required to fall consistently within a narrow composition range.

Continuous mixing processes are somewhat analogous to those discussed under fluid mixing. Metered quantities of the powders or granules are passed through a device that reduces both the scale and intensity of segregation, usually by impact or shearing action.

Barrel Type Continuous Mixer

In this mixer, the material is mixed under tumbling motion. The presence of baffles further enhances the mixing. When the material approaches the midpoint of the shell, a set of baffles

causes a part of the material to move backwards. Such a mechanism provides intense mixing of ingredients

Zig-zag Continuous Blender

It consists of several “V”-shaped blenders connected in series, when the blender is inverted, the material splits into two portions, one-half of the material moves backwards, while the other moves forward. In each rotation, a part of the material moves towards the discharge end

Mixer Selection

Mixer Property

An ideal mixer should produce a complete blend rapidly with as gentle mixing action as possible to avoid product damage. It should be dust tight, cleaned and discharged easily, and require low maintenance and low power consumption.

Rotating shell mixers suffer from poor cross-flow along the axis. The addition of baffles or inclining the drum on the axis increases cross-flow and improves the mixing action. In cubical and polyhedron-shaped blenders, due to their flat surfaces, the powder is subjected more to a sliding than a rolling action, a motion that is not conducive to efficient mixing. In double cone blenders the mixing pattern provides a good cross-flow with a rolling rather than sliding motion. The uneven length of each shell in twin-shell blender provides additional mixing action when the powder bed recombines during each revolution of the blender. Twin-shell and double-cone blenders are recommended for precision blending.

The shearing action that develops between moving blades and trough in agitator mixers serves to breakdown powder agglomerates. Ribbon mixers are not precision blenders and also suffer from the disadvantage of being more difficult to clean than the tumblers and having a higher power requirement.

The mechanical heat build-up and the relatively higher power requirement are the drawbacks also associated with sigma blade and planetary mixers. However, the shorter time interval necessary to achieve a satisfactory blend may offset these factors. Blendex provides efficient batch and continuous mixing for a wide variety of solids without particle size reduction and heat generation.

Material Property

Powders that are not free-flowing or that exhibit high forces of cohesion or adhesion between particles of similar or dissimilar composition are often difficult to mix owing to agglomeration.

The clumps of particles can be broken down in such cases by the use of mixers that generate high shear forces or that subject the powder to impact. The use of agitators preferably planetary and sigma blade are recommended for such powders.

For strongly cohesive materials, it is typically necessary to fragment agglomerates through the introduction of high shear, "intensification," devices such as agitators or mills that energetically deform grains on the finest scale.

THANK YOU

