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Mixing Part 1	عنوان المحاضرة باللغة الانجليزية
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محتوى المحاضرة

Mixing

Almost every pharmaceutical product contains more than one component, and this necessitates mixing or blending stages in their manufacturing process

mixing as a process “in which two or more ingredients in separate or roughly mixed condition are treated so that each particle of any one ingredient is as nearly as possible adjacent to a particle of each of the other ingredients

The term *blending* is synonymous with mixing, and *segregation* is the opposite

Mixing tends to result in a randomization of dissimilar particles within a system . This is to be distinguished from an ordered system in which the particles are arranged according to some iterative rule and thus follow a repetitive pattern

Mixing is a fundamental step in most process sequences, and is normally carried out:

1-To control heat and mass transfer

2-To secure uniformity of composition so that small samples withdrawn from a bulk material represent the overall composition of the mixture 3-To improve single phase and multi-phase systems

4-To promote physical and chemical reactions, such as dissolution, in which natural diffusion is supplemented by agitation

Mixing can be classified as positive, negative, or neutral

Positive mixing applies to the systems where spontaneous, irreversible and complete mixing would take place, by diffusion, without the expenditure of energy, provided time is unlimited , In general, positive mixtures, such as a mixture of two gases or two miscible liquids do not present any problems during mixing.

Negative mixing are generally more difficult to form and maintain, and require a higher degree of mixing ,any two-phase systems such as suspensions of solids in liquids, emulsions and creams tend to separate out quickly, unless energy is continually expended on them

Neutral mixing occurs when neither mixing nor de-mixing takes place unless the system is acted upon by an external energy input. Neutral mixtures are static in behavior, have no tendency to mix spontaneously or segregate spontaneously and include mixture of powders, pastes and ointments

Fluid MIXING

Flow Characteristics

Fluids may be generally classifies as Newtonian and non Newtonian, depending on the relationship between their shear rates and the applied stress.

Forces of shear are generated by interactions between moving fluids and the surfaces over which they flow during mixing.

The rate of shear may be defined as the derivative of velocity with respect to distance measured normal to the direction of flow

The viscosity is the ratio of shear stress to the shear rate

For Newtonian fluids, the rate of shear is proportional to the applied stress, and such fluids have a dynamic viscosity that is independent of flow rate.

While for non-Newtonian fluids apparent dynamic viscosity is a function of the shear stress

Fluid MIXING

Mixing Mechanisms

Mixing mechanisms for fluids fall essentially into four categories: bulk transport, turbulent flow, laminar flow, and molecular diffusion. Usually, more than one of these mechanisms is operative in practical mixing situations.

1-**Bulk Transport** The movement of a relatively large portion of the material being mixed from one location in a system to another location in a given system ,rotating blades and paddles are usually used

2-**Turbulent Mixing** The phenomenon of turbulent mixing is the direct result of turbulent fluid flow, which is characterized by a random fluctuation of the fluid velocity at any given point within the system

3-**Laminar Mixing** When two dissimilar liquids are mixed through laminar flow, the shear that is generated stretches the interface between them 4-**Molecular Diffusion** The primary mechanism responsible for mixing at the molecular level is diffusion, resulting from the thermal motion of the molecules

Equipments

A system for liquid mixing commonly consists of two primary components: (1) a tank or other container suitable for holding the material being mixed, and (2) a means of supplying energy to the system so as to bring about reasonably rapid mixing.

Power may be supplied to the fluid mass by means of an impeller, air stream, or liquid jet
Besides supplying power, these also serve to direct the flow of material within the vessel. Baffles, vanes, and ducts are also used to direct the bulk movement of material in such mixers, thereby increasing their efficiency.

When the material to be mixed is limited in volume so that it may be conveniently contained in a suitable mixer, *batch mixing* is usually more feasible, however, for larger volumes *continuous mixing* is preferred

Batch mixing

1-Impellers

Liquids are most commonly mixed by impellers rotating in tanks. These impellers are classified as (i) propellers, (ii) turbines and (iii) paddles. The distinction between impeller types is often made on the basis of the type of flow pattern they produce, or on the basis of the shape and pitch of the blades.

The flow pattern may be analyzed in terms of three components: 1) radial (perpendicular to the impeller shaft),

2) Axial or longitudinal (parallel to the impeller shaft),

3) tangential (tangential to the circle of rotation around the impeller shaft) . These may occur singly or in various combinations.

Propellers

Propellers of various types and forms are used, but all are essentially a segment of a multithreaded screw, that is, a screw with as many threads as the propeller blades Also, like the machine screws, propellers may be either right- or left-handed depending on the direction of slant of their blades

Although any number of blades may be used, the three-blade design is most commonly used with fluids

The blades may be set at any angle or pitch, but for most applications, the pitch is approximately equal to the propeller diameter

Propellers are most efficient when they run at high speeds in liquids of relatively low viscosity

Although some tangential flow does occur, the primary effect of a propeller is due to axial flow. Also, intense turbulence usually occurs in the immediate vicinity of the propeller

Turbines

They are usually distinguished from propellers in that the blades of the latter do not have a constant pitch throughout their length

When radial-tangential flow is desired, turbines with blades set at a 90-degree angle to their shaft are employed

With these type of impellers, a radial flow is induced by the centrifugal action of the revolving blades
.
Turbines having tilted blades produce an axial discharge quite similar to that of propellers

Because they lend themselves to a simple and rugged design, these turbines can be operated satisfactorily in fluids 1000 times more viscous than fluids in which a propeller of comparable size can be used

.
Paddles
Paddles are also employed as impellers and are normally operated at low speeds of 50 rpm or less

Their blades have a large surface area as compared
to the tank in which they are employed, a feature that permits them to pass close to the tank walls and effectively mix viscous liquids and semisolids which tend to cling to these surfaces

Circulation is primarily tangential, and consequently, concentration gradients in the axial and radial directions may persist in this type of mixer even after prolonged operation.

Operating procedures should take these characteristics into account ,With such mixers, for example, ingredients should not be layered when they are added to the mixing tank

2-Air Jets

Air jet devices involve sub-surface jets of air, or less commonly of some other gas, for

effective mixing of certain liquids.
Of necessity and for obvious reasons, the liquids must be of low viscosity, non foaming, nonreactive with the gas employed, and reasonably nonvolatile.

The jets are usually arranged so that the buoyancy of the bubbles lifts liquids from the bottom to the top of the mixing vessel.

This is often accomplished with the aid of draft tubes ,These serve to confine the expanding bubbles and entrained liquids, resulting in a more efficient lifting action by the bubbles, and inducing an upward fluid flow in the tube. This flow tends to circulate fluid in the tank, bringing it into the turbulent region in the vicinity of the jet.

The overall circulation in the mixing vessel brings fluid from all parts of the tank to the region of the jet itself. Here, the intense turbulence generated by the jet produces intimate mixing

3-Fluid Jets

They utilize liquids pumped at high pressure into a tank for mixing.

The power required for pumping can often be used to accomplish the mixing operation, either partially or completely.

In such a case, the fluids are pumped through nozzles arranged to permit a good circulation of material throughout the tank

In operation, fluid jets behave somewhat like propellers and they generate turbulent flow axially.

However, they do not themselves generate tangential flow, like propellers. Jets also may be operated simply by pumping liquid from the tank through the jet back into the tank

Continuous or In-line Mixers

The process of continuous mixing produces an uninterrupted supply of freshly mixed material, and is often desirable when very large volumes of materials are to be handled.
It can be accomplished essentially in two ways:
1-in a *tube or pipe* through which the material flows and in which there is very little back flow or recirculation,

2-or in a *mixing chamber* in which a considerable amount of holdup and recirculation occur

To ensure good mixing efficiency, devices such as vanes, baffles, screws, grids, or combinations of these are placed in the mixing tube.

Continuous or In-line Mixers

Mixing in such systems requires careful control of the feed rate of raw materials if a mixture of uniform composition is to be obtained.

The requirement of an exact metering in such a device results from the lack of recirculation, which would otherwise tend to average out concentration gradients along the pipe.

Where suitable metering devices are available, this method of mixing is very efficient. Little additional power input over that required for simple transfer through a pipe is necessary to accomplish mixing.

Practical Considerations

Vortexing

A vortex develops at the center of the vessel when liquids are mixed by a centrally-mounted vertical-shaft impeller. This particularly is characteristic of turbine with blades arranged perpendicular to the impeller shaft. These impellers tend to induce tangen-tial flow, which does not itself produce any mixing, except possibly near the tank walls where shear forces exist, instead, swirl and the vortex formation. This is true except at very low impeller speeds or at very high liquid viscosities (>20,000 cps), neither of which is normally encountered in practice in the pharmaceutical industry. When a vortex is formed, air is drawn into the impeller and is dispersed into the liquid, which is undesirable, as it may lead to foaming, especially if surfactants are present, and also because the full power of the impeller is not imparted to the liquid. The entrapped air also causes oxidation of the substances in certain cases and reduces the mixing intensity by reducing the velocity of the impeller relative to the surrounding fluid.

Vortixes may be avoided by

(i) changing arrangement of the impeller,

(ii) changing the tank geometry,

(iii) using a push-pull propeller,

(iv) using baffles and

(v) using diffuser ring.