PHARMACEUTICAL ENGINEERING

Reactors and Fundamentals of Reactors Design for Chemical Reaction

Dr. Sanju Nanda
M.Pharm, Ph.D. (IIT Delhi)
Dept. of Pharmaceutical Sciences
M.D. University
Rohtak – 124001
Haryana

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Introduction

A *Chemical reaction* is a process that results in the conversion of chemical substances. The substance or substances initially involved in a chemical reaction are called *reactants*. These reactants are characterized by a chemical change and they yield one or more products. These products are generally different from the original reactants. Chemical reactions may be of different nature depending on the type of reactants, type of product desired, conditions and time of the reaction, for example, *synthesis, decomposition, displacement, percipitation, isomerization, acid-base, redox* or o*rganic reactions.* These reactions are being given in Table 1, stating their area of utility, advantages, limitations and examples.

Table 1 : Types Of Chemical Reactions

Type of Reaction		Area of Utility	Advantages	Limitations	Examples
A. Inorganic	Combination	To synthesize new compounds	Two or more reactants make on industrially useful compound	Some undesirable byproducts may be produced	$N_2 + 3H_2 \rightarrow 2NH_3$ Nitrogen Hydrogen Ammonia
	Decomposition	Breakdown of larger, unuseful compounds/ complexes into smaller useful compounds	More number of useful products generated	High energy involved	Fractional distillation of petroleum and coke
	Substitution	Salt formation New compounds formation	Obtaining compounds of choice which are otherwise available with difficulty	Sometimes lead to unwanted/undesired substitution	$2KI + Pb(No_3)_2 \rightarrow$ Pot. Iodide Lead Nitrate $2KNO_3 + PbI$ Pot. Nitrate Lead Iodide
	Isomerization	A chemical compound undergoes a structural rearrangement without any change in the atomic composition	Physico-chemical properties may be modified. New compounds may be obtained	Sometimes give undesirable compounds	Thalidomide
B. Organic	Esterification	A reaction between an organic acid and an alcohol forming an ester and water.	Important pharmaceutical compounds including prodrugs can be prepared	Limited to reaction between an organic acid or acid chloride	$CH_3CH_2OH + CH_3COOH \rightarrow$ Methanol Acetic Acid $CH_3CH_2OOCH_3 + H_2O$ Methyl Acetate
	Hydrolysis	A large molecule is split into two smaller molecules in the presence of water	New compounds may be formed	Just having water present as the solvent does not make a reaction a hydrolysis reaction	$CH_3COOCCH_2CH_3 + H_2O$ Methyl propionate $CH_3OH + CH_3CH_2COOH$ Methanol Propionic acid
	Hydrogenation	Hydrogen is added across a double bond or a triple bond	New saturated compounds may be synthesized	Needs the presence of a catalyst	$CH_2=CH_2+H_2 \rightarrow CH_3CH_3$ Ethene Ethane

	Substitution	One small group in a molecule is replaced by another small group	New compounds may be synthesized	Being an organic compound, substitution reactions are not so easy	$CH_3CH_2OH+HCl \rightarrow CH_3CH_2Cl+$ Ethyl alcohol Ethyl chloride H_2O

Chemical reactors are vessels designed to contain chemical reactions[2]. It is the site of conversion of raw materials into products and is also called the heart of a chemical process. The design of a chemical reactor where bulk drugs would be synthesized on a commercial scale would depend on multiple aspects of chemical engineering. Since it is a very vital step in the overall design of a process, designers ensure that the reaction proceeds with the highest efficiency towards the desired output, producing the highest yield of product in the most cost effective way.

Reactors are designed based on features like *mode of operation* or *types of phases present* or the *geometry of reactors*. They are thus called:

- *Batch* or *Continuous* depending on the mode of operation.
- *Homogeneous* or *Heterogeneous* depending upon the phases present.

They may also be classified as :

- Stirred Tank Reactor, or
- Tubular Reactor, or
- Packed Bed Reactor, or
- Fluidized Bed Reactor,

depending upon the flow pattern and manner in which the phases make contact with each other. A detailed comparison of various chemical reactors is tabulated in Table-2.

Table 2 : Comparison Of Chemical Reactors

S. No.	Type of Reactor	Principle of Working	Advantages	Limitations	Area of Application
1.	Batch Reactor	All reactants are added at the commencement and the product withdrawn at the completion of the reaction. They are conducted in tanks attached with impellers, gas bubbles or pumps.	• Suitable for small scale production • Suitable for processes where a range of different products or grades is to be produced in the same equipment • Suitable for reactions requiring long reaction times • Suitable for reactions with superior selectivity	• Not suitable for large batch sizes • It is a closed system in which once the reactants are added in the reactor, they will come out as products only after the completion of the reaction	Batch processes are used in chemical (inks, dyes, polymers) and food industry
2.	Continuous	One or more fluid	• Highly flexible	• More	Chemical

	Stirred Tank Reactor (CSTR)	reagents are introduced into a tank reactor equipped with an impeller while the reactor effluent is recovered. A stepped up concentration gradient exists	device • By products may be removed in between the reaction • It is economically beneficial to operate several CSTRs in series or in parallel. • Reaction can be carried out in horizontal as well as vertical reactors	complex and expensive than tubular units • All calculations performed with CSTRs assume perfect mixing • At steady state, the flow rate in must equal the flow rate out, otherwise the tank will overflow or go empty	industry especially involving liquid/gas reactions
3	Plug Flow Reactor (PFR)	One or more fluid reagents are pumped through a pipe or tube. These are characterized by continuous gradients of concentration in the direction of flow	• Higher efficiency than a CSTR of the same volume • PFRs may have several pipes or tubes in parallel • Both horizontal and vertical operations are common • They can be jacketed • Reagents may be introduced at locations even other then inlet	• Not economical for small batches	The tubular reactor is specially suited to cases needing considerable heat transfer, where high pressures and very high or very low temperatures occur

Batch Process

A process in which all the reactants are added together at the beginning of the process and products removed at the termination of the reaction is called a batch process. In this process, all the reagents are added at the commencement and no addition or withdrawal is made while the reaction is progressing (Fig. 1). Batch processes are suitable for small production and for processes where a range of different products or grades is to be produced in the same equipment for example, pigments, dye stuff and polymers.

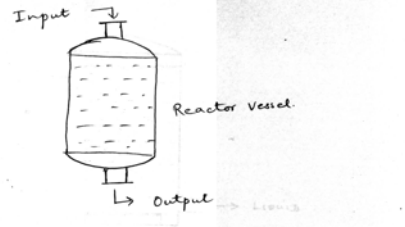

Figure 1: Batch Process

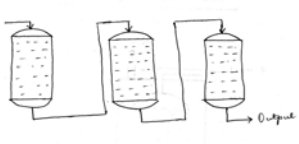

Figure 2: Continuous Process

Continuous Process

A process in which the reactants are fed to the reactor and the products or byproducts are withdrawn in between while the reaction is still progressing (Fig. 2). For example, Haber Process for the manufacture of Ammonia. Continuous production will normally give lower production costs as compared to batch production, but it faces the limitation of lacking the flexibility of batch production. Continuous reactors are usually preferred for large scale production.

Semi Batch Process

Process that do not fit in the definition of batch or a semibatch reactor is operated with both continuous and batch inputs and outputs and are often referred to as *semi continuous* or *semi-batch*. In such semi-batch reactors, some of the reactants may be added or some of the products withdrawn as the reaction proceeds. A semi-continuous process can also be one which is interrupted periodically for some specific purpose, for example, for the regeneration of catalyst, or for removal of gas for example, a fermentor is loaded with a batch, which constantly produces carbon dioxide, which has to be removed continuously. Another example is chlorination of a liquid.

Catalytic Processes

Most of the chemical reactions either proceed in the presence of catalysts or increases their yield in the presence of catalysts. A *catalyst* is a substance that, without itself undergoing any permanent chemical change, increases the rate of a reaction. The rate of a catalytic reaction is proportional to the amount of catalyst the contact with a fluid phase reagents. This is proportional to the exposed area, efficiency of diffusion of reagents in and products out, type of mixing (turbulent, etc). The assumption of perfect mixing cannot be assumed. A catalytic reaction pathway is often multistep with intermediates that are chemically bound to the catalyst. Since the chemical binding is also a chemical reaction, it may affect the reaction kinetics. The behaviour of the catalyst is also a consideration. Particularly in high temperature petrochemical processes, catalysts are deactivated by sintering, coking and similar processes.

Homogeneous Reactions

Homogeneous reactions are those in which the reactants, products and any catalyst used form one continuous phase; for example, *gaseous* or *liquid.* Homogeneous gas phase reactors will always be operated continuously. *Tubular* (Pipe line) reactors are normally used for homogeneous gas phase reactions; for example, in the thermal cracking of petroleum, crude oil fractions to ethylene, and the thermal decomposition of *dichloroethane* to *vinyl chloride.* Homogeneous liquid phase reactors may be batch or continuous. Batch reactions of single or miscible liquids are almost invariably done in stirred or pump around tanks. The agitation is needed to mix multiple feeds at the start and to enhance heat exchange with cooling or heating media during the process.

Heterogeneous Reactions

In a heterogeneous reaction two or more phases exist and the *overriding* problems in the reactor design is to promote mass transfer between the phases.
The possible combination of phases are :

1) **Liquid-Liquid** :- Liquid reactions of industrial importance are fairly numerous. For example, reactions such as the nitration of toluene or benzene with mixed acids, emulsion polymerizations, saponification, etc. Such reactions can be carried out in any kind of equipment that is suitable for physical extraction, including mixer-settlers

and towers of various kinds, for example *empty* or *packed, still* or *agitated*, etc. Mechanically agitated tanks are favoured because the interfacial area can be made large as much as 100 times that of spray towers. When agitation is sufficient to produce a homogeneous dispersion and the rate varies with further increase of agitation, mass-transfer rates are likely to be significant.

2) **Liquid-Solid** :- The solid may be a reactant or catalyst. For example, platinum acts as a catalyst in the hydrogenation of oils. In the design of reactors for liquids in the presence of granular catalysts, account must be taken of heat transfer, pressure drop and contacting of the phases and sometimes provision for periodic or continuous regeneration of deteriorated catalyst. Several different kinds of vessel configurations for continuous processing are in commercial use. Most solid catalytic processes employ fixed beds. Although fluidized beds have the merit of nearly uniform temperature and can be designed for continuous regeneration, they cost more and more, difficult to operate, require extensive provisions for dust recovery, and suffer from back mixing.

3) **Liquid-Solid Gas** :- In reactions involving gas, liquid and solid phases, the solid phase is generally a porous catalyst. For example, gasoline cracking using zeolite catalysts. It may be in a fixed bed or it may be suspended in fluid mixture. In general, the reaction occurs either in the liquid phase or at the liquid / solid interface. In *trickle bed* reactors both phases usually flow down, the liquid as a film over the packing. In *flooded reactors*, the gas and liquid flow upward through a fixed bed, the *slurry reactors* keep the solids in suspension mechanically; the overflow may be a clear liquid or a slurry, and the gas disengages from the vessel. In fluidized bed reactors a stable bed of solids is maintained in the vessel and only the fluid phases flow through, except for entrained very fine particles.

4) **Solid-Solid** :-Many reactions of solids are industrially feasible only at elevated temperatures which are often obtained by contact with combustion gases, particularly when the reaction is done on a large scale. For example, decomposition of azides, diazo compounds and nitramines. A product of reaction also is often a gas that must diffuse away from a remaining solid, sometimes through a solid product. Thus thermal and mass-transfer resistances are major factors in the performance of solid reactions.

5) **Gas-Solid** :- In some reactions, the solid either takes part in the reaction or act as a catalyst. For example, finely divided nickel is used in the preparation of nickel carbonyl (b.p. 42^0C). Other examples of solid /gas reactions include combustion of solid fuels, atmospheric corrosion, manufacture of hydrogen by action of steam on iron, chlorination of ores of uranium, titanium, zirconium and aluminum, conversion of ferrous oxide to magnetic ferric oxide in contact with reducing atmosphere of CO in combustion gases.

6) **Gas-Liquid** :- In certain processes, liquid may either take part in the reaction or act as catalyst. Gas/liquid reaction processes are generally employed by the industry either for the purpose of gas purification or the removal of relatively small amounts of impurities such as CO_2, CO, SO_2, H_2S, NO and others from air, natural gas, hydrogen for ammonia, synthesis, etc. This type of reaction is also utilized in the manufacture of pure products such as sulphuric acid, nitric acid, nitrates, phosphates, adipic acid,

etc. or processes like hydrogenation, halogenation oxidation, nitration, alkylation, etc. Bio-chemical processes such as fermentation oxidation of studies sludges, production of proteins etc. are also examples of gas/liquid reactions. There could be at least three ways in which the reaction between a gas and a liquid may be made to react, that is, the gas may be either dispersed as bubbles in the liquid (Fig. 3), the liquid may be dispersed as droplets in the gas (Fig. 4) or the liquid and gas are brought together as their films over a packing or wall (Fig. 5). The choice between these models is critical and is dependent on factors. Such as magnitude and distribution of the residence times of the phases, the power requirements, the scale of the operation, etc.

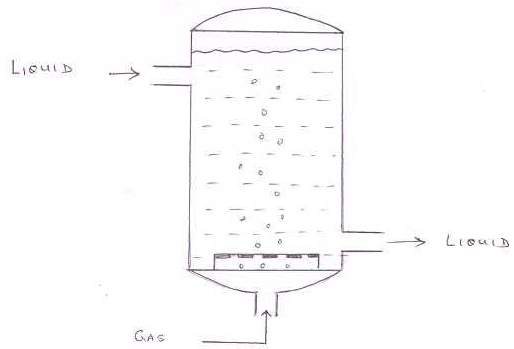

Figure 3: Bubble Tower

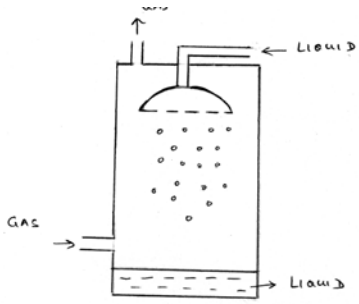

Figure 4: Spray Tower

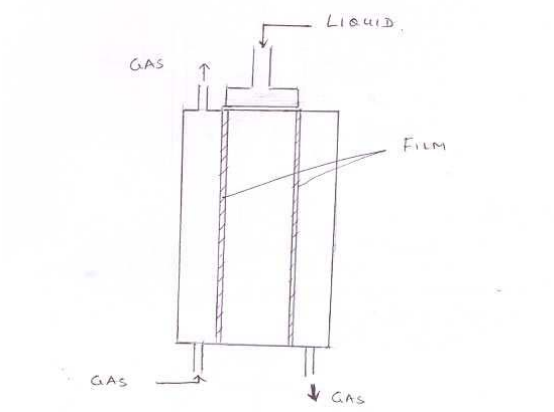

Figure 5: Falling Liquid Film

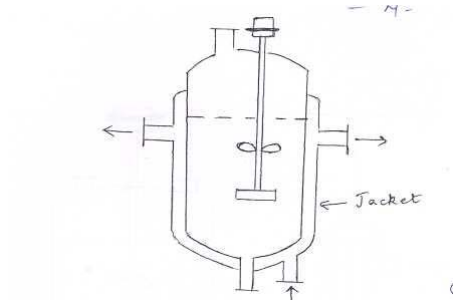

Figure 6: CSTR Jacketed

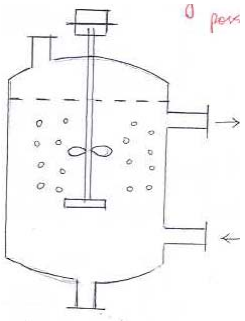

Figure 7: CSTR with Internal coils

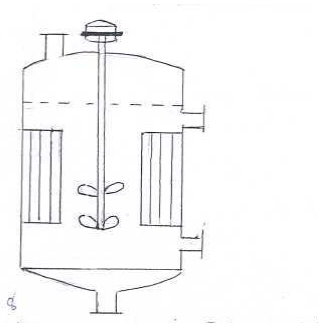

Figure 8: CSTR with Internal Tubes

Reactor Geometry

The reactors used for established processes are usually complex designs which have been developed and evolved over a period of years to suit the requirements of the process, and are

unique designs. However, it is convenient to classify reactor designs into the following broad categories.

A. **Stirred Tank Reactors** :- Stirred tank agitated reactors consist of a tank fitted with a mechanical agitator and a cooling jacket or coils (Fig. 6, Fig. 7, Fig. 8, Fig. 9, Fig. 10). They are operated as batch reactors or continuous reactors. Several reactors may be used in series.

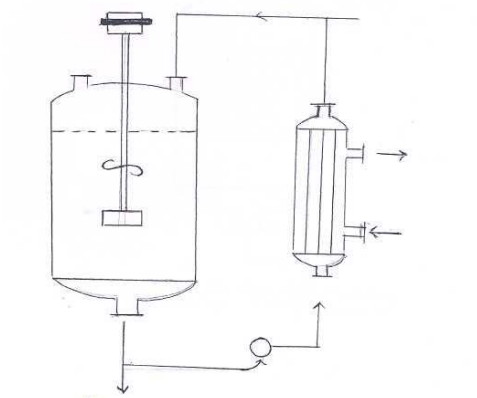

Figure 9: CSTR with External Heat Exchanger

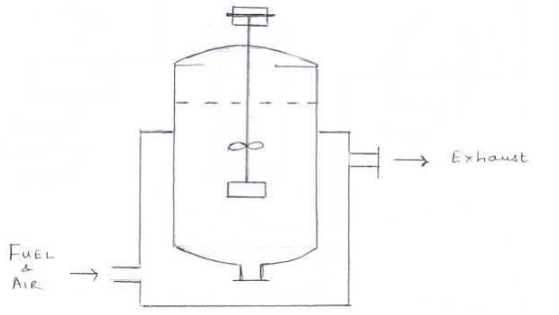

Figure 10: CSTR with Air Heater

The *stirred tank reactor* can be considered the basic chemical reactor; modeling on a large scale the conventional laboratory flask. Tank sizes range from a few litres to several thousand litres. They are used for homogeneous and heterogeneous liquid-liquid and liquid-gas reactions and for reactions that involve freely suspended solids, which are held in suspension by the agitation. As the degree of agitation is under the designers control, stirred tank reactors are particularly suitable for reactions where good mass transfer or heat transfer is required.

When operated as a continuous process the composition in the reactor is constant and the same as the product stream and except for very rapid reactions, this will limit the conversion that can be obtained in one stage.

The power requirements for agitation will depend on the degree of agitation required and will range from about $0.2kW/m^3$ for moderate mixing to $2kW/m^3$ for intense mixing.

B. **Tubular Reactors** : Tubular reactors are generally used for gaseous reactions, but are also suitable for some liquid phase reactions. If high heat transfer rates are required small diameter tubes are used to increase the surface area to volume ratio. Several tubes may be arranged in parallel, connected to a manifold or fitted into a tube sheet in a similar arrangement to a shell and tube heat exchangers. For high temperature reactions the tubes may be arranged in a furnace.

C. **Packed Bed Reactors** :- There are two basic types of packed bed reactor; those in which the solid is a reactant and those in which the solid is a catalyst (Fig.11 and Fig. 12).

In chemical process industries, the emphasize is mainly on the designing of catalytic reactors. Industrial packed bed catalytic reactors range in size from small tubes, a few centimeters diameter to large diameter packed beds. Packed-bed reactors are used for gas and gas-liquid reactions. Heat-transfer rates in large diameter packed beds are

poor therefore, where high heat-transfer rates are required, fluidised beds should be considered.

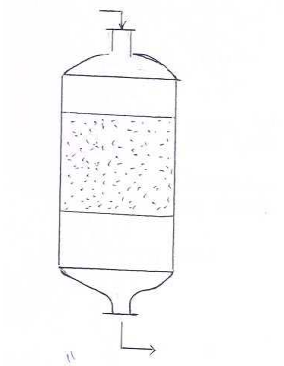

Fig: 11: Packed Bed Reactor

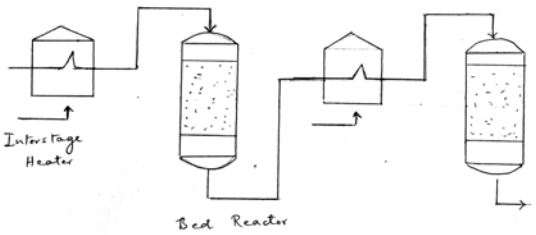

Fig. 12: Multibed Reactors with Interstage Heaters

D. **Fluidised Bed Reactors** :- A fluidized-bed reactor (Fig. 13) is a combination of the two most common, packed-bed and stirred tank, continuous flow reactors. It is very important to chemical engineering because of its excellent heat and mass transfer characteristics. The essential features of a fluidised bed reactor is that the solids are held in suspension by the upward flow of the reacting fluid. This promotes high mass and heat transfer rates and good mixing. Heat-transfer coefficients in the order of 200 $W/m^2\ ^0C$ to jackets and internal coils are typically obtained. The solids may be a catalyst, a reactant in fluidized combustion processes or an inert powder, added to promote heat transfer.Though the principal advantage of a fluidised bed over a fixed bed is the higher heat transfer rate, fluidised beds are also useful where it is necessary to transport large quantities of solids as part of the reaction processes, such as where catalysts are transferred to another vessel for regeneration.Fluidisation can only be used with relatively small sized particles, that is less than 300μm. This is the limitation of the process.

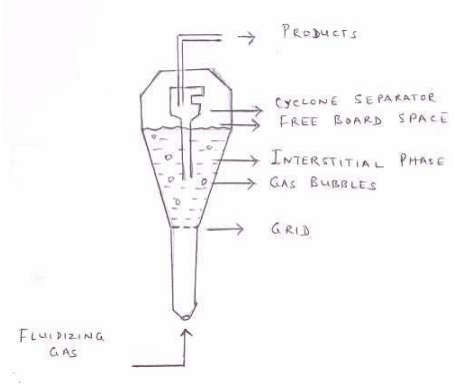

Figure 13: Flow Distribution in a Fluidized bed

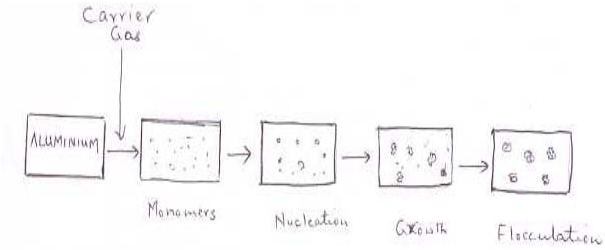

Figure 14: Aerosol Nanoparticle Reactor

Fundamentals of Reactor Design

The design of a chemical reactor deals with multiple aspects of chemical engineering. *Chemical reactions*, *chemical energetics* and equations/laws of thermodynamics play an important role in the selection and design of chemical reactors.

Chemical Reactions: Brief representation of the chemical change in terms of symbols and formulae of the reactants and products is called a *chemical equation*. For example, when zinc reacts with hydrochloric acid, zinc chloride and hydrogen are produced.

Zinc + Hydrochloric acid → Zinc chloride + Hydrogen

If symbols and formulae of various reactants and products are used, the above reaction may be represented as :

$Zn + HCl \rightarrow ZnCl_2 + H_2$ ……..…(1)

As per Dalton's atomic theory that atoms are neither created nor destroyed during chemical changes, therefore the number of atoms of various elements should be equal on the reactant side as well as on the product side. Equations such as above, in which no attempt has been made to equalize the number of atoms of various elements on both the sides are called *Skeleton equations*. Therefore, in order to equitize the number of atoms of various elements, various species are multiplied with appropriate numbers. This process is called balancing of a chemical equation. The above equation (1) can be balanced by multiplying HCl with 2

$Zn + 2\ HCl \rightarrow ZnCl_2 + H_2$ …….(2)

A chemical equation in which the number of atoms to each element is equal on the reactant side and product side is called a *balanced equation*.

A chemical equation, therefore must fulfill the following conditions:

a) It should represent, a true chemical change, and if a reaction is not possible between certain substances, it cannot be represented by a chemical equation.

b) It should be balanced

c) It should be molecular, i.e. all the species should be represented in their molecular form. For example, elementary gases like hydrogen, oxygen, etc., should be represented as H_2 and O_2.

A chemical equation has both qualitative as well as quantitative significance. Qualitatively, a chemical equation tells us the names of the various reactants and products. Quantitatively, it expresses

a) The relative number of molecules of the reactants and products taking part in the reaction.
b) The relative number of moles of reactants and products.
c) The relative volumes of gaseous reactants and products.

For example :

$2H_2 + O_2 \rightarrow 2H_2O$ ……..(3)

Qualitatively, it tells us that hydrogen and oxygen reacts to form water. Quantitatively, it conveys the following information.

a) Two molecules of hydrogen react with one molecule of oxygen to form two molecules of water.

b) Two moles of hydrogen react with one mole of oxygen to form two moles of water.

c) 4 g of hydrogen react with 32 g of oxygen to form 36 g of water.

d) Two volumes of hydrogen react with one volume of oxygen to form two volumes of water vapour.

The chemical equation can be made more informative by incorporating the following changes:

a) The physical states of reactants and products can be indicated by using the abbreviations, for example, (s) for solids, (l) for liquid, (g) for gas and (aq) for aqueous solution. For example,

$$\mathbf{Zn(s) + 2HCl(aq) \rightarrow ZnCl_2(aq) + H_2(g) \ldots\ldots\ldots\ldots..(4)}$$

b) In order to indicate the strength of acid or base, *dil* for dilute or *conc* for concentration is written before the formula of acid or base.

$$\mathbf{Zn(s) + 2\ dil\ HCl(aq) \rightarrow ZnCl_2(aq) + H_2(g) \ldots\ldots\ldots\ldots.(5)}$$

c) The reaction conditions such as presence of catalyst, temperature, pressure, etc., may be written above the arrow between the reactants and products.

$$\mathbf{2SO_2\ (g) + O_2(g) \xrightarrow{V_2O_5,\ 775^0K} 2SO_3(g) \ldots\ldots\ldots\ldots..(6)}$$

d) Heat change taking place during the reaction may be expressed in any one of the following two ways.

$$\mathbf{N_2(g) + 3H_2(g) \rightarrow 2NH_3(g) + 93.6\ KJ \ldots\ldots\ldots\ldots\ldots\ldots\ldots.(7)}$$

Or $\mathbf{N_2(g) + 3H_2(g) \rightarrow 2NH_3(g);}$

$$\mathbf{\Delta\ H^* = -9.36KJ}$$

*ΔH = change in *enthalpy*, that is heat evolved or absorbed in a reaction at constant temperature and pressure. *Enthalpy* is the total energy associated with any system which includes its internal energy and also energy due to environmental factors such as pressure-volume conditions. It is denoted by H.

Chemical equations give the quantitative relationship between the reactants and the products. This quantitative information can be utilized to carry out variety of calculations which are required many a times, to assess the economic viability of the chemical process.

Calculations based on the quantitative relationship between the reactants and the products are also referred to as *Stoichiometry.* The word stoichiometry is derived from the Greek words *Stoicheron* meaning *element* and *metron* meaning measure. *Stoichiometry is* therefore, that *area of chemistry and chemical technology on which determination of quantities of reactants and products of chemical reaction is based.*

Chemical Energetics: Chemical reactions are always associated with energy changes. Quite often, the energy change accompanying a chemical reaction is more significant than the reaction itself. The branch of science which deals with the energy changes associated with chemical reactions is called *chemical energetics*. The energy changes occurring during the chemical reactions may not always appear as heat energy, but also as *electrical* energy, *work energy* and *radiant energy* as well. Thus, it is evident that chemical reactions are

accompanied by energy changes appearing in different forms. These energy changes take place because during chemical reactions certain bonds are cleaved and certain new bonds are formed. Energy is consumed during cleavage of bonds while energy is released during the formation of bonds.

Thermodynamics: Since the bond energy varies from one bond to another, the chemical reactions are always accompanied by absorption or release of energy. Most of the time the energy is in the form of heat. Therefore, it becomes imperative that some concepts of thermodynamics may be understood. *Thermodynamcis* literally means conversion of heat into work and vice-versa because *therm* refers to heat and *dynamics* refers to movement. *Thermodynamics* may, therefore, be defined as *the branch of science which deals with the quantitative relationship between heat and other forms of energies*. When thermodynamics of chemical processes is studied, it is often referred to as *chemical thermodynamics*.

Thermodynamics is primarily based upon *three* fundamental generalisations, popular as *Laws of Thermodynamics*. They are :

1) First Law of Thermodynamics, which deals with the equivalence of different forms of energies.

2) Second Law of thermodynamics, which deals with the direction of chemical change.

3) Third Law of thermodynamics, which helps to evaluate the thermodynamic parameter like entropy.

Therefore, the design of an industrial chemical reactor must satisfy the following requirements:

1. **The chemical factors :** *The kinetics of the reaction.* The design must provide sufficient residence time for the desired reaction to proceed to the required degree of conversion.

2. **The mass transfer factors** : With hetereogeneous reactions, the reaction rate may be controlled by the rates of diffusion of the reacting species, rather than the chemical kinetics.

3. **The heat transfer factors** : The removal or addition of the heat of reaction.

4. **The safety factors** :- The confinement of hazardous reactants and products and the control of the reaction and the process conditions.

5. **Economic factors** : Minimum amount of money should be required to purchase and operate. Normal operating expenses include energy input, energy removal, raw material costs, labour, etc. Energy changes can come in the form of heating or cooling, pumping, agitation, etc. The need to satisfy these are interrelated and often contradictory factors makes reactor design a complex and difficult task. However, in many instances one of the factors will predominate and will determine the choice of reactor type and the design method.

Design Procedure and Reactor Designing

An industrial chemical reactor is a complex device in which heat transfer, mass transfer, diffusion and friction must be considered and it must be safe and controllable. In large vessels, problem of mixing of reactants, flow distribution, residence time distribution and

efficient utilization of the surface of porous catalysts also arise. A successful commercial unit is an economic balance of all these factors.

A general procedure for reactor design is outlined below:

1. The kinetic and thermodynamic data on the desired reaction is initially collected. Values will be needed for the rate of reaction over a range of operating conditions, for example, pressure, temperature, flow rate and catalyst concentration. This data may be normally obtained from either laboratory or pilot plant studies.
2. Data on physical properties is required for the design of the reactor. This may be either estimated, or collected from the literature or obtained by taking laboratory measurements.
3. The rate controlling mechanism which has a predominant role is then identified, for example, *kinetic*, *mass* or *heat* transfer.
4. A suitable reactor type is then chosen, based on experience with similar studies or from the laboratory and pilot plant work.
5. Selection of optimal reaction conditions is initially made in order to obtain the desired yield
6. The size of the reactor is decided and its performance estimated. Since exact analytical solutions of the design relationship are rarely possible, semiemperical methods based on the analysis of idealized reactors are used.
7. Materials for the construction of the reactor is/are selected.
8. A preliminary mechanical design for the reactor including the vessel design, heat transfer surfaces etc., is made.
9. The design is optimized and validated
10. An approximate cost of the proposed and validated design is then calculated.

In choosing the reactor conditions, and optimizing the design, the interaction of the reactor design with the other process operations must not be overlooked. The degree of conversion of raw materials in the reactor will determine the size and the cost of any equipment needed to separate and recycle unreacted materials. In these circumstances the reactor and associated equipment must be optimized as a unit.

Reactor Designing – Mathematical Models

Chemical reactors are vessels designed to contain chemical reactions. The design of a chemical reactor deals with multiple aspects of chemical engineering including mathematical modeling. *A model of a reaction process is a set of data and equation that is believed to represent the performance of a specific vessel configuration* (mixed, plug flow, laminar, dispersed, etc.). Chemical engineers, design reactors to maximize net present value for the given reaction. Designers ensure that the reaction proceeds with the highest efficiency towards the desired output product, producing the highest yield of product. The equations used in mathematical modeling include the stoichiometric relations, rate equations, heat and material balances and auxiliary relations such as those of mass transfer, pressure variation, residence time distribution, etc.

The data not only describe physical and thermodynamic properties but also the economic factors. Correlations of heat and mass – transfer rates are fairly well developed and can be incorporated in models of a reaction process, but the chemical rate data must be determined individually. Since equipments are now widely available to obtain such data, hence an initial exploratory work can be carried out.

Once fundamental data is obtained, the goal is to develop a mathematical model of the process, which may be further utilized to explore possibilities such as *product selectivity, start-up and shut down behaviour, vessel configuration, temperature, pressure and conversion profiles,* etc.

Any mathematical model has two components, the *symbols* in which it is expressed and their relationship to the quantities in the real world and the *equations* that link the symbols and through which the values of certain variables are computed. These two elements normally co-evolve, but they are often separated for the sake of presentation into the parameter and variable definitions and their equations.

Principle: First a mechanism is assumed and then a model is designed accordingly, for example, whether the reaction is steady or unsteady, completely mixed, or plug flow or laminar or with dispersion or with bypass or recycle or dead space, etc.

Then, for a differential element of space and/or time, the elements of conservation are formulated and put together.

Inputs + Sources = Outputs + Sinks + Accumulations

Any transport properties are introduced through known correlations together with the parameters of specified rate equations. *The model can be used to find the performance under various conditions, or its parameters can be evaluated from experimental data.*

Basic Elements of Reactor Designing

Reactions are carried out as *batches* or with *continuous streams* through a vessel. There are two main basic vessel types, viz.;

- Tank Reactor – a tank
- Tubular Reactor – a pipe or tube

Most commonly, reactors are run at a *steady-state*, but can also be operated in a *transient state*. Transient state is a state in which the key process variables like residence time, volume, temperature, pressure or concentration of chemical species, etc., change with time. Such a situation generally arises when either the reactor is purchased new or is brought back in operation after maintenance or inoperation. Chemical reactors may be designed keeping in view the various process variables. Key process variables include:

- Residence Time Distribution (τ)
- Volume (v)
- Temperature (T)
- Pressure (P)
- Concentrations of chemical species (C_1, C_2, C_3------C_4)
- Heat transfer coefficients (h, U)

Residence Time Distribution (RTD) (τ): The *residence time distribution (RTD)* of a chemical reactor or vessel is a description of the time that different fluid elements spend inside the reactor. The concept was first proposed by MacMullin and Weber in 1935, but was not used extensively until P.V. Danckwerts analyzed a number of important RTDs in 1953[3].

RTD will vary from one reactor type to another. For example, an ideal plug flow reactor has a fixed residence time. Any fluid that enters the reactor at time 't' will exit the reactor at time t + τ, where τ is the residence time of the reactor.

Flow reactors are distinguished by the degree of mixing of successive inputs. The ideal situations are

1) Complete mixing :- For example *Continuous Stirred Tank Reactor (CSTR) (Fig. 6), and*
2) No axial mixing – For example, *Plug Flow Reactor (PFR)*

Real reactors deviate more or less from these ideal behaviours. Deviations may be detected with RTDs obtained with the aid of tracer tests. The commonest models are combinations of CSTRs and PFRs in series and/or parallel. Thus, a stirred tank may be assumed completely mixed in the vicinity of the impeller or a plug flow near outlet.

Heat Transfer

Temperature affects rates of reaction, degradation of catalysts and equilibrium conversion. Many reactors with fixed beds of catalysts pellets have divided beds, with heat transfer between the individual sections. Such units can take advantage of initial high rates at high temperatures and higher equilibrium conversions at lower temperatures.

Since reactors come in a variety of configurations with a variety of operating modes and may handle mixed phases, the design of provisions for temperature control draws on a large body of heat transfer theory and data.

Mass Balance

A *mass balance* (also called a *material balance*) is an accounting of material entering and leaving a system[7]. Fundamental to the balance is the conservation of mass principle, i.e., that matter can not disappear or be created. Mass balances are used, for example, to design chemical reactors, analyse alternative processes to produce chemicals, in pollution dispersion models, etc. In environmental monitoring the term *budget calculations* is used to describe mass balance equations where they are used to evaluate the monitoring data (comparing input and output, etc.). The dynamic energy budget theory for metabolic organisation makes explicit use of time, mass, and energy balances.

The mass that enters a system must (conservation of mass principle) either leave the system or accumulate within the system, i.e.

$$IN = OUT + ACC \quad \textbf{……..(8)}$$

where IN denotes what enters the system, OUT denotes what leaves the system and ACC denotes accumulation within the system (which may be negative or positive). Mass balances are often developed for total mass crossing the boundaries of a system, but they can also focus on one element (e.g. carbon) or chemical compound (e.g. water). When mass balances

are written for specific compounds, number of individuals in a population, etc. rather than for the total mass of the system, a production term (PROD) is introduced such that

IN + PROD = OUT + ACC **……(9)**

The PROD describes the chemical reaction rates, the difference between births and deaths, etc. PROD might be positive or negative, just as for ACC.

Mass balances are either *Integral Mass Balances* or *Differential Mass Balances*. An integral mass balance is a black box approach and focus on the overall behaviour of a system whereas a differential mass balances focuses on mechanisms within the system (which in turn affect the overall behavior).

Integral Mass Balance is made by initially identifying the system boundaries, that is, how the system is connected to the rest of the world and how the rest of the world influences the system. For example, for a tank reactor the walls of the tank are the system boundaries and the outer world influences the system through the inlet and outleet. *Differential mass balance* is described by assuming the interior of the systems, for example, a perfectly mixed (homogeneous) system. Based on these basic descriptions of the system and its boundaries, reactor models are described. They are either

1. Ideal (continuously stirred) Batch reactor
2. Ideal tank reactor, also named Continuously Stirred Tank Reactor (CSTR)
3. Ideal Plug Flow Reactor (PFR)

Ideal Batch Reactor: It is a closed system. The mass balance for a substance 'A' becomes

IN + PROD = OUT + ACC

$$0 + r_{\mathrm{A}}V = 0 + \frac{dn_{\mathrm{A}}}{dt} \quad \textbf{……(10)}$$

where r_A denote the rate at which substance A is produced, V is the volume (which may be constant or not), n_A the number of moles (n) of substance A.

In a fed-batch reactor some reactants/ingredients are added continuously or in pulses.

Ideal tank reactor/Continuously Stirred Tank Reactor: It is an open system. A lake can be regarded as a tank reactor and lakes with long turnover times (e.g. with a low flux to volume ratio) can for many purposes be regarded as continuously stirred (e.g. homogeneous in all respects). The mass balance becomes

IN + PROD = OUT + ACC

$$Q_0 * C_{\mathrm{A},0} + r_A * V = Q * C_{\mathrm{A}} + \frac{dn_{\mathrm{A}}}{dt} \quad \textbf{…….(11)}$$

where Q_0 and Q denote the volumetric flow in and out of the system respectively and $C_{A,O}$ and C_A the concentration of A in the inflow and outflow respective.

Ideal Plug Flow Reactor (PFR): It is an open system with no mixing along the reactor but perfect mixing across the reactor. It is often used for systems like water pipes, if the flow is turbulent. When a mass balance is made for a tube, an infinitesimal part of the tube is first considered and a mass balance is made using the ideal tank reactor model. That mass balance is then integrated over the entire reactor volume to obtain:

$$\frac{d(Q * C_A)}{dV} = r_A \quad \text{.....(12)}$$

More complex problems: In reality, reactors are often non-ideal, in which combinations of the reactor models above are used to describe the system. Not only chemical reaction rates, but also mass transfer rates may be important in the mathematical description of a system, especially in heterogeneous systems. As the chemical reaction rate depends on temperature it is often necessary to make both an energy balance (often a heat balance rather than a full fledged energy balance) as well as mass balances to fully describe the system. A different reactor models might be needed for the energy balance: A system that is closed with respect to mass might be open with respect to energy because since heat may enter the system through conduction.

Types of Reactor Models

There are *three* main basic models used to estimate the most important process variables of different chemical reactors.

- Batch Reactor Model (Batch)
- Continuous Stirred-Tank Reactor Model (CSTR) and
- Plug Flow Reactor Model (PFR)

These basic models may be modified as per requirement of a chemical process.

Batch Reactor Models: Batch reactors are used in batch processes. Batch processes are suited to small production rates, to long reaction times, or to reactions, where they may have superior selectivity, as in some polymerizations.

They are conducted in tanks with stirring of the contents by internal impellers, gas bubbles or pump around. Control of temperature is done with the help of jackets, reflux condensers or pump around through an exchanger.

Batch processes are currently used in the chemical and food process industries. Their automation and optimization pose difficult issues mainly because it is necessary to operate concurrently with countinous (algebric or differential equations) and discrete (state machines) models. Andreu et al[14], have tried to analyse how techniques developed in the field of discrete manufacturing systems (DMS) can be extended to batch systems.

A *semi-batch reactor* is operated with both continuous and batch inputs and outputs. A fermentor, for example, is loaded with a batch which constantly produces carbon dioxide, which has to be removed continuously. Similarly, in a reaction like *chlorination,* where one of the reactant is gas (chlorine), if it is introduced continuously, most of it bubbles off, therefore a continuous feed of gas is injected into the batch of a liquid.

Large daily production rates are mostly conducted in continuous equipment, either in a series of stirred tanks or in units in which some degree of plug flow is attained.

Continuous Stirred Tank Reactor (CSTR) Model : In a CSTR, one or more fluid reagents are introduced into a tank reactor equipped with an impeller while the reactor effluent is recovered. The impeller stirs the reagents to ensure proper mixing. Therefore, it can be seen that in these reactors, reactants are continuously fed to the first vessel, they overflow through the others in succession, while being thoroughly mixed in each vessel. Though the composition is uniform in individual vessels, but a stepped concentration gradient exists in the system as a whole.

The average amount of time spent by a discrete quantity of reagent inside the tank or the *residence time* can be obtained by simply dividing the volume of the tank by the average volumetric flow rate through the tank. The expected completion rate of the reaction, in percent can be calculated using chemical kinetics.

Some important aspects of the CSTR are :

- All calculations performed with CSTRs assume perfect mixing.
- The reaction proceeds at the reaction rate associated with the final (output) concentration.
- At steady state, the flow rate in must equal the mass flow rate out, otherwise the tank will overflow or go empty (transient state).
- It is often economically beneficial to operate several CSTRs in series or in parallel. A series of five or six vessels may behave like a plug flow reactor. This allows the first CSTR to operate at a higher reagent concentration and therefore a higher reaction rate. It is also possible that instead of being in distinct vessels, the several stages of a CSTR battery can be put in a single shell.
- If horizontal, the multistage reactor is compartmented by vertical wires of different heights, over which the reacting mixture cascades.
- When the reactants are of limited miscibilities and have a sufficient density difference, the vertical staged reactor lends itself to *counter current operation*. This can be advantageous for reversible reactions.
- A small fluidized bed is essentially completely mixed. A large commercial fluidized bed reactor is a nearly uniform temperature, but the flow patterns consist of mixed and plug flow and in-between zones.

The *CSTR model* is used to estimate the key unit operation variables when using a continuous agitated tank reactor to reach a specified output. *The mathematical model works for all fluids : liquids, gases and slurries.*

Perfect Mixing: This is a fair assumption due to the fact that it merely requires the region of variable composition at the inlet area is very small when compared to the entire reactor contents and the time required to mix tank contents is very small when compared to the residence time of the reactor. This is required due to the strong dependence of the reaction rate on the concentration of the reagent species.

[accumulation] = [in] – [out] + [generation] **……(13)**

$$\frac{d\,Ni}{dt} = Fio - Fi + V_{vi}r \text{ - - - - - - - (i)} \qquad \textbf{……(14)}$$

Where F_{io} is the molar flow rat of species 'i'
Ni no. of species 'i'
vi is the stoichiometric coefficient
r is the reaction rate

As the temperature increases, the rate of reaction also changes.

Plug Flow Reactor (PFR) Model: In a PFR, one or more fluid reagents are pumped through a pipe or tube. It is also referred to as Tubular Flow Reactors (TFRs).

- PTRs may have several pipes or tubes in parallel,. The reactants are charged continuously at one end and products are removed at the other end.
- The chemical reaction proceeds as the reagents travel through the PFR.
- In this type of reactor, the reaction rate is *gradient*, that is, at the inlet to the PFR the rate is very high, but as the concentrations of the reagents decrease and the concentration of the product(s) increases the reaction rate slows. Normally a steady state is attained.
- Both horizontal and vertical operations are common.
- When heat transfer is needed, individual tubes are jacketed or shell and tube construction is used. In the latter case, the reactants may be on either the shell or the tube side.
- The reactant side may be filled with solid particles, either catalytic (if required) or inert, to improve interphase contact in heterogeneous reactions.
- Large diameter vessels with packing or trays may approach plug flow behaviour and are widely employed.
- Some of the configurations in use are axial flow, radial flow, multiple shell with built in heat exchangers, horizontal, vertical and so on.

Some important aspects of the PFR are :

- All calculations performed with PFRs assume no upstream or downstream mixing, as implied by the term "plug flow".
- Reagents may be introduced into the PFR at locations in the reactor other than the inlet. In this way a higher efficiency may be obtained, or the size and cost of the PFR may be reduced.
- A PFR typically has a higher efficiency than a CSTR of the same volume. That is, given the same space-time, a reaction will proceed to a higher percentage completion in a PFR than in a CSTR.

For most chemical reactions, it is impossible for the reaction to proceed to 100% completion. The rate of reaction decreases as the percent completion increases until the point where the system reaches dynamic equilibrium (no net reaction, or change in chemical species occur). The equilibrium point for most systems is less than 100% complete. For this reason a separation process such as *distillation* often follows a chemical reactor in order to separate any remaining reagents or by products from the desired product. These reagents may sometimes be reused at the beginning of the process, such as in the *Haber process*.

The PFR model is used to estimate the key unit operation variables when using a continuous tubular reactor to reach a specified output. The mathematical model works for all fluids :

liquids, gases and slurries. In a PFR the fluid passes through a coherent manner, so that the *residence time 'τ'*, is the same for all fluid elements. The coherent fluid passing through the ideal reactor is known as a plug. As a plug flows through a PFR, the fluid is perfectly mixed in the radial direction but not in the axial direction (forwards or backwards). Each plug of differential volume is considered as a separate entity (practically a batch reactor) As it flows down the tubular PFR.

Application of PFRs (Also see Table 2): PFRs are used to model the chemical transformation of compounds as they are transported in systems resembling pipes. Plug flow reactors are used for some of the following applications:

- Large scale reactions
- Fast reactions
- Homogeneous or Heterogeneous Reaction
- Continuous Production
- High Temperature Reactions

An ideal pug flow reactor has a fixed residence time, that is, any fluid (plug) that enters the reactor at time 't' will exist the reactor at time 't+τ', where 'τ' is the residence time of the reactor. A real plug flow reactor has a residence time distribution that is a narrow pulse around the mean residence time distribution.

Plug flow reactors have a high volumetric unit conversion run for long periods of time without labour, and have excellent heat transfer. The limitations encountered with plug flow reactors are that temperatures are difficult to control and can result in undesirable temperature gradients. It is more expensive.

Catalytic Reactors

Although catalytic reactors are often implemented as plug flow reactors, their analysis requires more complicated treatment. The rate of a catalytic reaction is proportional to the amount of catalyst the reagents contact. In case of solid phase catalyst and fluid phase reagents, the rate of reaction is proportional to the exposed area, efficiency of diffusion of reagents in and products out, and turbulent mixing or lack thereof.

A catalytic reaction pathway, in fact, is often multi step reaction because not only the initial reactants will bound to the catalyst but even some intermediates may bind to the catalyst and pose as a chemical reaction.

The behaviour of the catalyst is also important in the kinetics of this reaction particularly in high temperature petrochemical processes, catalysts are deactivated by sintering, coking and similar processes.

Application of plug flow reactors in allied fields based on new technologies:

- **Plug- flow reactors for biomass conversion:** The experiments are conducted in a continuous high pressure plant made from stainless steel. The pressure can be set to a maximum of 35 MPa. There are several reactor sizes available so that residence times from 0.5 to 600 seconds can be covered. In order to reach temperatures above 300 °C two electrically heated reactors can be used. They cover residence times up to 250 resp. 180 seconds. The feed solutions are delievered via HPLC-pumps.

- **Aerosol nanoparticle plug flow reactors (APFR):** There is considerable interest in the synthesis and use of nanosized particles for a variety of applications including superalloys and thick film conductors for the electronics industry. Furthermore, other areas of interest include measurements of magnetic susceptibility, far-infrared transmission and nuclear magnetic resonance. For these systems, it is necessary to produce fine particles of controlled size. Particle sizes can typically be in the range from 10 to 500 nm.

Owing to their size, shape, and high specific surface area, these particles can also be used in pigments in cosmetics, membranes, photo catalytic reactors, catalysts and ceramic and catalytic reactors. Examples of uses of nanoparticles include SnO_2 for carbon monoxide gas sensors, TiO_2 for fiber optics, SiO_2 for fumed silica and optical fibers, carbon for carbon black fillers in tyres, iron for recording materials, nickel for batteries and to a lesser extent palladium, magnesium, bismuth and others; all these materials have been synthesized in aerosol reactors. In the bioarea, nanoparticles are used to prevent and treat wound infections in artificial bone implants, and for use in imaging the brain.

Example of APFR : production of aluminum particles (Fig. 14). A stream of argon gas saturated with aluminum vapor is cooled in a APFR, with a diameter of 18 mm and a length of 0.5 m, from 1600°C at a rate of 1000°C/sec. As the gas stream flows through the reactor, the nucleation and growth of aluminum particles take place. Flow rate of the carrier gas is 2 dm^3/min and the pressure inside the PFR is 1 atm (1.013 Pa). Moving with the gas velocity U, the cooling rate inside the reactor is 1000 K/s and hence the temperature profile down the reactor is given by:

$$\frac{dT}{dx} = -\frac{1000}{U} \qquad \text{……..(15)}$$

As it moves down the reactor the gas gets cooled and becomes supersaturated. Thus super saturation leads to the nucleation of particles. This nucleation is a result of molecules colliding, escaping (evaporating) and agglomerating until a critical nucleus size is reached and a particle is formed. As these particles move down the supersaturated gas molecules condense on the particles causing them to grow in size.

Conclusion

Pharmaceutical substances are basically chemicals showing therapeutic effects. After their safety, efficacy and bioavailability is established, these substances are given the status of drugs by the drug regulatory bodies and allowed to be produced on industrial scale for commercial purposes. These drugs which are required to be synthesized in bulk are produced in special vessels called reactors. An industrial chemical reactor is a complex device in which heat transfer, mass transfer, diffusion and friction may occur along with chemical reaction and it must be safe and controllable. The design of these chemical reactors require a good understanding of multiple aspects of pharmaceutical engineering because in large vessels, question of mixing of reactants, flow distribution, residence time distribution and efficient utilization of the surface of porous catalysts also arise. The selection of the type of reactor will be dictated by the type of reaction type, type of reactants, time of reaction and conditions of reaction. A knowledge of various aspects of pharmaceutical (chemical) engineering would help the engineers to design, and select such reactors in which the resources are optimally utilized and the reaction proceeds with highest efficiency giving the best possible yields.

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