Unit 1
Polymers

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Contents

- Introduction
- Classification
- Properties
- Advantages and application of polymers in formulation of controlled release drug delivery systems.

Polymers : Definition

- Polymers are high molecular mass macromolecules composed of repeating structural units derived from monomers.
- The word ‘polymer’ comes from the Greek words poly (meaning ‘many’) and meros (meaning ‘parts’).
- In a polymer, various monomer units are joined by **strong covalent bonds**.
- Polymers can be natural as well as synthetic.
- Ex.-Polythene, rubber, and nylon 6, 6 , silk, wool, DNA, cellulose and proteins
- **Monomers** are simple, reactive molecules that combine with each other in large numbers through covalent bonds to give rise to polymers. For example, ethene, propene, styrene, vinyl chloride.
- POLYETHYLENE = (ETHYLENE+ ETHYLENE+......)n Where n = 4,000

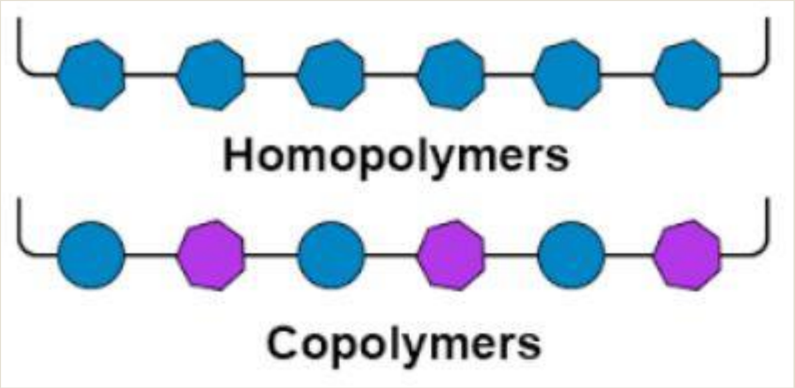
Polymerization

- Polymerization is the process of forming high molecular mass (103 − 107 u) macromolecules, which consist of repeating structural units derived from monomers.
- In a polymer, various monomer units are joined by strong covalent bonds.
- The process by which the monomer molecules are linked to form a big polymer molecule
- As a chemical process, the synthesis of polymers can occur by either of two methods:

1. Addition polymerization
2. Condensation polymerization

Homopolymer& Copolymer

- A **homopolymer** is defined as a polymer that has the same monomer unit in the chain. Whereas **polymer** which consists of more than one kind of monomers is called a **copolymer**.
- **Examples** of **homopolymer** are PVC with vinyl chloride units, polypropylene with propylene units, Polymethyl-methacrylate.
- **Examples** of **Copolymer** polyethylene-vinyl acetate (PEVA), nitrile rubber, and acrylonitrile butadiene styrene (ABS).



Polymers for Control Drug Delivery System

Applications of polymers range from their

- use as binders in tablets
- viscosity builders and flow controlling agents in liquids, suspensions and emulsions.
- as film coatings to mask the unpleasant taste of a drug,
- to enhance drug stability
- to **modify drug release characteristics** and
- Protection of the drug from enzymatic degradation - particularly applicable to peptide and protein drugs

Polymers for Control Drug Delivery System

- Polymer(natural or synthetic) is combined with a drug so that the drug is released from CDDS in predesigned manner.
- The release of the active agent may be constant over a long period,
- it may be cyclic over a long period, or
- it may be triggered by the particular environment or
- other external events.

Polymeric Drug Delivery Systems

- Incorporate drug into a polymeric matrix
- Release drug at a known rate over a prolonged duration
- Release drug directly to the site of action
- Constant release - often the goal - difficult to achieve
- Deliver drug such that concentration in tissue is in appropriate range
- Protection of the drug from enzymatic degradation - particularly applicable to peptide and protein drugs

Polymer: Classification

1. Classification based on source/origin
2. Classification based on monomer
3. Classification based on thermal response
4. Classification based on mode of formation
5. Classification based on structure

Polymer: Classification based on source

1. **Natural polymers** -Polymers which are isolated from natural materials are called as natural polymers. E.g. Silk, Wool, Natural rubber, Cellulose, Starch, Proteins etc.

2. **Semi-synthetic polymers –** The polymers obtained by simple chemical treatment of natural polymers to improve their physical properties like lustrous nature, tensile strength are called semisynthetic polymers E.g. Cellulose acetate, Cellulose nitrate

3. **Synthetic polymers** - Human-made **polymers that** are prepared in laboratory is known as Synthetic Polymer. Example - Buna-S, Buna-R, Nylon, Polythene, Polyester Nylon, Terylene, Polyethylene, Synthetic rubber, Nylon, PVC, Bakelite, Teflon etc.

Polymer: Classification based on monomer

- **Homo Polymers** -A polymer consist of identical monomers is called homo polymer.
  - E.g. Polyethylene, PVC, Polypropylene, Nylon 6
- **Co Polymers** -A polymer consist of monomers of different chemical structure are called copolymers.
  - E.g. Nylon 6,6

Polymer: Classification based on thermal response

Thermoplastic Polymers

- They are easily moulded in desired shapes by heating and subsequent cooling at room temperature.
- They are soft in hot and hard on cooling.
- They can be linear or branched chain polymers. E.g. PE, PVC, PS, PP

Thermosetting Polymers

- This polymer is hard and infusible on heating.
- These are not soft on heating under pressure and they are not remolded.
- These are cross linked polymers and are not reused. E.g. Bakelite

Polymer: Classification based on mode of formation

1. **Addition Polymers**

- The polymers formed by the addition of monomers repeatedly without removal of by products are called addition polymers.
- These polymers contains all the atoms of monomers hence their molecular weight are integral multiple of monomer unit. E.g. Teflon, Polyethylene, Polypropylene, PVC.

2. **Condensation Polymers**

- They are formed by the combination of two monomers by removal of small molecules like H_2O, Alcohol or NH_3.
- Their molecular mass is not the integral multiple of monomer units.
- They have ester and amide linkage in their molecules. E.g. Polyamides(Nylons), Polyesters(PET)

Polymer: Classification based on structure

Linear Polymers

- In these polymers monomers are linked with each other and form a long straight chain.
- These chains has no any side chains.
- Their molecules are closely packed and have high density, tensile strength, and melting point. E.g. HDPE, Nylons

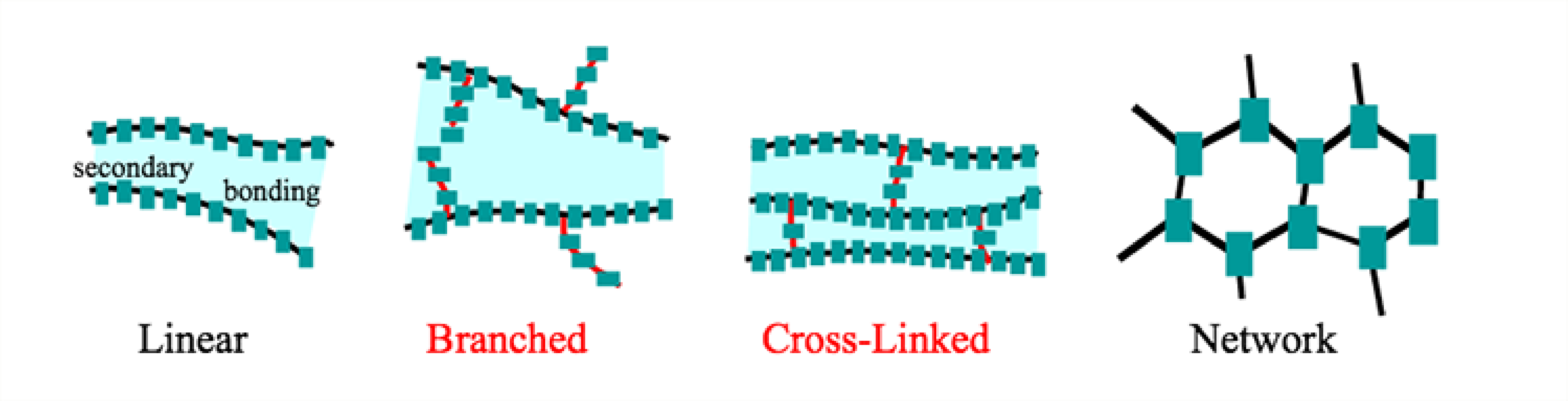
Branched Polymers

- They have a straight long chain with different side chains.
- Their molecules are irregularly packed hence they have low density, Tensile strength and melting point. E.g. LDPE, LLDPE

Cross-linked Polymer

- In these monomeric units are linked together to constitute a 3D network.
- The links involved are called cross links.
- They are hard, rigid and brittle due to their network structure. E.g. Bakelite, Melamine, Formaldehyde resins, Vulcanized rubber

Polymer: Classification based on structure



Types of Polymers

- **Elastomers:** These are rubber-like solids weak interaction forces are present. For example, Rubber.
- **Fibres:** Strong, tough, high tensile strength and strong forces of interaction are present. For example, nylon -6, 6.
- **Thermoplastics:** These have intermediate forces of attraction. For example, polyvinyl chloride.
- **Thermosetting polymers:** These polymers greatly improve the material's mechanical properties. It provides enhanced chemical and heat resistance. For example, phenolics, epoxies, and silicones.

Types of Polymers

◦ On the basis of the type of the backbone chain, polymers can be divided into:

- **Organic Polymers**: Carbon backbone.
- **Inorganic Polymers**: Backbone constituted by elements other than carbon.

Types of Polymers

Based on Bio-stability:

1. **Biodegradable Polymers**-The polymers which are degraded and decayed by microorganisms like bacteria are known as **biodegradable polymers**. These types of polymers are used in surgical bandages, capsule coatings and in surgery. For example, Poly hydroxybutyrate co vel [PHBV] polyesters, proteins, carbohydrates, etc
2. **Nonbiodegradable Polymers-** After a certain period of time, the natural **polymers** degrade on their own but synthetic **polymers** do not. These are **non-biodegradable polymers** and are resistant to environmental degradation processes and are accumulated as solid waste materials. For example, ethyl cellulose, HPMC, acrylic polymer

Properties of Polymers

- **Physical properties of polymers**: include molecular weight, molar volume, density, degree of polymerization, crystallinity
- **Mechanical properties of polymers:**Tensile Strength, Young’s Modulus,Percent Elongation, Toughness

Degree of Polymerization and Molecular Weight

- The **degree of polymerization (DP)**-n in a polymer molecule is defined as the number of repeating units in the polymer chain.
- For example, $-(-CH_2 - CH_2-)-n$. Where n is the number of monomeric units in a macromolecule or **polymer**
- The **molecular weight** of a polymer molecule is the product of the degree of polymerization and the molecular weight of the repeating unit
- DP affects properties of the polymer: higher DP increases mechanical strength but also increases viscosity in the fluid state, which makes processing more difficult

Degree of Polymerization and Molecular Weight

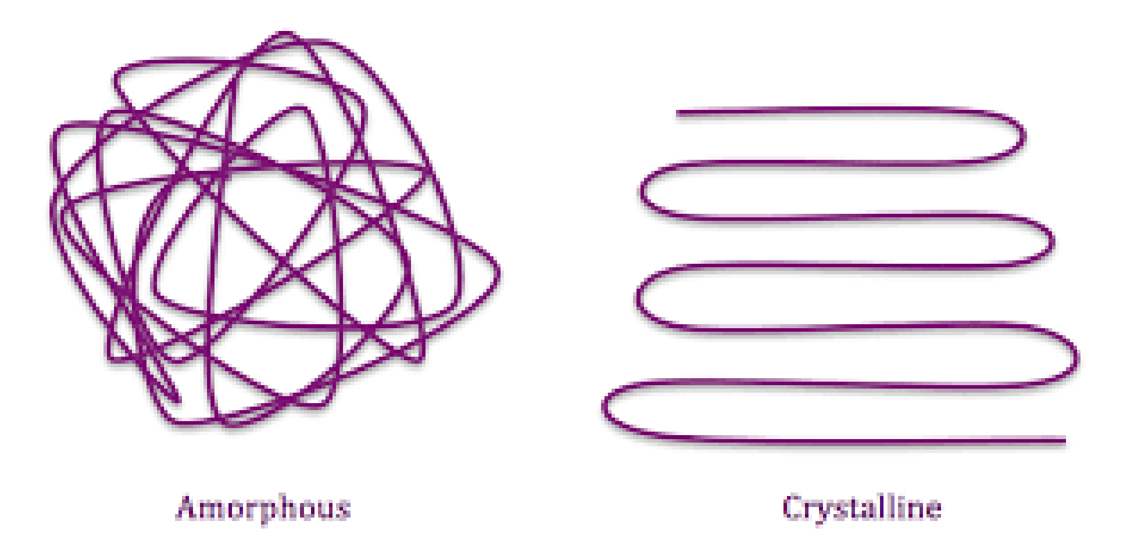
- The physical properties (such as transition temperature, viscosity, etc.) and mechanical properties (such as strength, stiffness, and toughness) depend on the molecular weight of polymer.
- The **lower the molecular weight**, lower the transition temperature, viscosity, and the mechanical properties. Due to increased entanglement of chains with increased molecular weight, the polymer gets higher viscosity in molten state, which makes the processing of polymer difficult.

Polymer	DP(n)	MW
Polyethylene	10,000	300,000
Polyvinylchloride	1,500	100,000
Nylon	120	15,000
Polycarbonate	200	40,000

http://www.me.nchu.edu.tw/lab/CIM/www/courses/Manufacturing%20Processes/Ch08-Polymers-Wiley.pdf

Polymer Crystallinity

1. Crystalline and
2. Amorphous Polymers



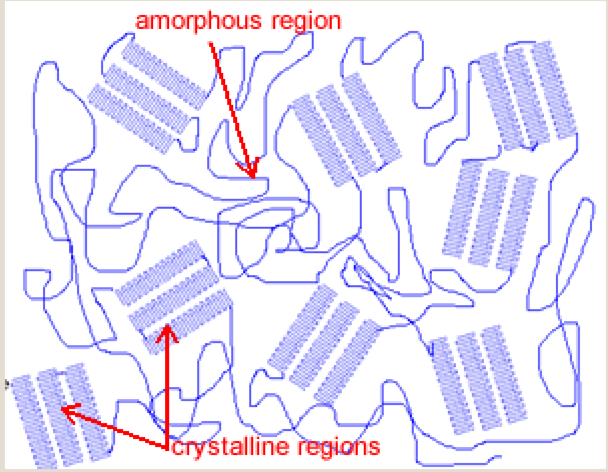
Polymer Crystallinity

Crystalline

- A well-ordered **polymer** is considered **crystalline**. The opposite is an **amorphous polymer**.
- The more **crystalline** a **polymer**, the more regularly aligned its chains. Increasing the degree of **crystallinity** increases hardness and density.

Amorphous

- **polymers** that do not exhibit any crystalline structures in X-ray or electron scattering experiments.
- They form a broad group of materials, including glassy, brittle and ductile **polymers**
- Lamellar crystalline form in which the chains fold and make lamellar structure arranged in the regular manner and amorphous form in which the chains are in the irregular manner. The lamellae are embedded in the amorphous part and can communicate with other lamellae via tie molecules



http://www.dynamicscience.com.au/tester/solutions1/chemistry/crystallinestructures.html

Glass Transition Temperature Tg

- At low temperature, amorphous polymer are in frozen state as the molecules of the polymer are not able to move significantly. In this state, the polymer is brittle, hard and rigid analogous to glass and called as **glassy state**.
- when this polymer is heated, the polymer chains are able to wiggle around each other, and the polymer becomes soft and flexible similar to rubber. This state is called the **rubbery state.**
- **The temperature at which the glassy state makes a transition to rubbery state is called the glass transition temperature Tg.**
- Note that the glass transition occurs only in the amorphous region, and the crystalline region remains unaffected during the glass transition in the semi-crystalline polymer.

Glass Transition Temperature Tg

Glass transition temperature is the **temperature** at which 30–50 carbon chains start to move. At the **glass transition temperature**, the amorphous regions experience **transition** from rigid state to more flexible state making the **temperature** at the border of the solid state to rubbery state.

The value of glass transition temperature depends on several factors such as

- **Molecular weight**-Tg is increased with the molecular weight
- **Plasticizers** (are low molecular weight materials added to polymers to increase their chain flexibility) reduce the intermolecular cohesive forces between the polymer chains, which in turn decrease Tg
- Intermolecular Forces. Strong intermolecular forces cause higher Tg.
- **Cross-links** -restrict rotational motion between chains and raise the glass transition temperature. Hence, higher cross-linked molecule will show higher Tg than that with lower cross-linked molecule
- **Stiffening groups** (such as amide, sulfone, carbonyl, p-phenylene etc.) in the polymer chain reduces the flexibility of the chain, leading to higher glass transition temperature.

Melting Point & Glass Transition Temperature

Glass Transition	Melting
Property of the amorphous region	Property of the crystalline region
Below T_g: Disordered amorphous solid with immobile molecules	Below T_m: Ordered crystalline solid
Above T_g: Disordered amorphous solid in which portions of molecules can wiggle around	Above T_m: Disordered melt
A second order transition	A first-order transition

https://www.slideshare.net/ArchanaAnish/polymer-properties-and-characterisation

Mechanical Properties of Polymers

- Tensile Strength
- Young's Modulus /Modulus of Elasticity /Tensile Modulus
- Percent Elongation
- Toughness

Tensile Strength:

Strength is the stress required to break the sample.

Types of the strength-

- tensile (stretching of the polymer),
- compressional (compressing the polymer),
- flexural (bending of the polymer),
- torsional (twisting of the polymer), impact (hammering)

The polymers follow the following order of increasing strength:

linear < branched < cross-linked < network

Factors Affecting the Strength of Polymers

- **Chain length** - the longer the chains the stronger the polymer
- **Side groups** - polar side groups give stronger attraction between polymer chains, making the polymer stronger
- **Molecular Weight**: The tensile strength of the polymer rises with increase in molecular weight
- **Cross-linking**: The cross-linking restricts the motion of the chains and increases the strength of the polymer.
- **Crystallinity:** The crystallinity of the polymer increases strength, because in the crystalline phase, the intermolecular bonding is more significant.

Young's Modulus (Modulus of Elasticity or Tensile Modulus):

- Young's Modulus is the ratio of stress to the strain in the linearly elastic region
- Elastic modulus is a measure of the stiffness of the material.

- E = Tensile Stress(σ)/ Tensile Strain(ε)

Percent Elongation to Break (Ultimate Elongation)

- The change length over original length is called elongation.
- It measures the percentage change in the length of the material before fracture.
- It is a measure of ductility.
- When the elongation is high , material is elastic.
- When the elongation is low, material is called brittle.

Toughness

- **Toughness** of a plastic is measured by its resistance to impacts.
- It is the ability of a material to resist both fracture and deformation.
- The toughness of a material is given by the area under a stress–strain curve.

Characteristics of Ideal Polymer

1. Should be inert and compatible with the environment.
2. Should be non-toxic.
3. Should be easily administered.
4. Should be easy and inexpensive to fabricate.
5. Should have good mechanical strength
6. Should be biocompatible
7. Should be biodegradable

Polymer: Advantages & Disadvantages

Advantages

1. Polymers have played an important role in the advance drug delivery technology by providing controlled release of therapeutic agents in constant doses over long periods, cyclic dosage, and tunable release of both hydrophilic and hydrophobic drugs.

Polymer: Application

- **Polymers** are **used in** almost every area of modern living. Grocery bags, soda and water bottles, textile fibers, phones, computers, food packaging, auto parts, and toys all contain **polymers**.
- Polymers have played indispensable roles in the preparation of pharmaceutical products.
- Their applications range widely from **material packaging** to fabrication of the most sophisticated drug delivery devices.
- In **tablet** the **polymer** are **used** as a Binder and Disintegrants. Binders which bind the powder particle in a damp mass various **polymer** are **used** are Ethyl cellulose, HPMC, Starch, Gelatin, polyvenylpyrrolidine. Disintegrates like Starch, cellulose, Alginates, polyvenylpyrrolidine, sodium CMC which decrease the time of dissolution and gives fast action of drug.
- Chitosan's film forming abilities lend itself well as a coating agent for conventional solid dosage forms such as tablets.

Polymer: Application

- **Capsules-**The various polymer are used in the capsule as the plasticizer on which the flexibility and strength of the Gelatin are depend on it .The release rate of the Capsule are controlled by using the various type of polymer.
- Natural polymer like Shellac and zein,
- For biphasic system are like emulsion, suspension use various polymer are used as dispersing agents
- **Transdermal Drug Delivery Systems (Patches)**
  In the formulation of Transdermal Patches various polymer are used. The baking material also prepared from the polymer for supporting of drug in drug reservoir.
- Microparticles- microcapsules and microspheres
- Nanoparticles- nanocapsules and nanospheres

Polymers for Controlled Release

These are some of the first materials selected for delivery systems bases on their intended non-biological physical properties:

- Polyurethanes for elasticity
- Polysiloxanes for insulating ability
- Polymethyl methacrylate for physical strength and transparency
- Polyvinyl alcohol for hydrophilicity and swelling
- Polyvinyl pyrrolidone for suspension capabilities

Current Polymers used in Controlled Drug Delivery

These polymers became usable in controlled delivery due to their inert physical characteristics and being free of leachable impurities

- Poly 2-hydroxy ethyl methacrylate
- Poly N-vinyl pyrrolidone
- Polyvinyl alcohol
- Polyacrylic acid
- Polyethylene glycol
- Polymethacrylic acid