POLYMERIC BIOMATERIALS

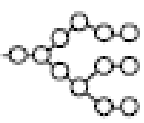
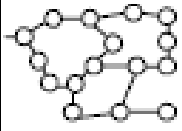
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Human beings dream of life everlasting. But most of them want it on earth and not in heaven.

INTRODUCTION

1. Polymer as name suggests is many mers (small molecules or repeating units) joining together under suitable condition to form a long chain (a heavy molecule). The process of forming a long chain of a heavy molecule from small molecules is called polymerization. The polymerization can be done by condensation (water is condensed out) or by addition (by rearranging bonds within each monomer). Polymer can be linear, branched or cross linked as shown in table below .

Polymer can be obtained by linking of one type of mers (monomers) or more than two types of mers. Hence copolymers are polymers made form two of more types of mers. The degree of polymerization (DP) is defined as average number of mers (repeating units) per molecule (long chain)*i.e.*, Molecular weight of polymerization = $DP \times$ molecular weight of mers. The possible arrangements of copolymers can be :–

S.N.	Type	Mer or Repeating unit	Linking
1	Linear polymer		
2	Branched polymer		
3	Crossed Linked		

(a) Random

(b) Alternating

(c) Block

(d) Graft



2. **Poly dispersity Index (PDI).** The ratio of weight average molecular weight to the number average molecular weight of any polymer is called polydispersity index and is denoted by PDI.

$$i.e.\ \text{PDI} = \frac{\overline{M}w}{\overline{M}n}$$

where $\overline{M}w$ = Weight average molecular weight

$\overline{M}n$ = Number average molecular weight

$$\overline{M}n = \frac{\sum NiMi}{\sum Ni} = \frac{N_1M_1 + N_2M_2 + \ldots}{N_1 + N_2 + \ldots}$$

where Ni = No. of molecules having molecular weight Mi

N_1 = Molecules have molecular weight M_1

N_2 = molecules have molecular weight M_2 and so on.

$$\overline{M}w = \frac{\sum NiMi^2}{\sum NiMi} = \frac{N_1M_1^2 + N_2M_2^2 + \ldots}{N_1M_1 + N_2M_2}$$

PDI gives an idea about the molecular weight dispersion. Therefore if PDI = 1 *i.e.*, $\overline{M}n = \overline{M}w$, then no dispersion in the system occurs and complete polymerisation has occurred without formation of other products. So in medicinal application, PDI should be unity to avoid any side reactions or side effects due to detachment of byproducts weakly adhered in the polymer.

Example: What is number and weight average molecular weight of polymer? Two monodisperse polymer samples with number average and molecular weight (*a*) 10,000 adn (*b*) 20,000 were weakly adhered in the polymer were mixed. Prepare two samples (1) by taking two parts of (*a*) and one part of (*b*) and (2) by taking one part of (*a*) and two part of (*b*). Calculate number and weight average molecular weight of mixture 1 and 2. (UPTU 2005-06)

Solution: Number average molecular weight. The arithmatic mean of molecular weight of all the polymeric chains present in the polymeric disperse. It can be given as total mass of polymeric disperse divided by the total number of molecules present. It is denoted by $\overline{M}n$

$$\overline{M}n = \frac{\Sigma N_i M_i}{\Sigma N_i} = \frac{N_1M_1 + N_2M_2 + \ldots}{N_1 + N_2 + \ldots}$$

Weight average molecular weight. In this various molecular species are taken proportion to their weights. It is denoted by $\overline{M}w$.

$$\overline{M}w = \frac{\Sigma W_i M_i}{\Sigma W_i} = \frac{W_1M_1 + W_2M_2 + \ldots.}{W_1 + W_2 + \ldots.}$$

But $Wi = Ni\,Mi$

$$\text{Hence } \overline{M}w = \frac{\Sigma N_iM_i^2}{\Sigma N_iM_i}$$

$$= \frac{N_1M_1^2 + N_2M_2^2 \ldots\ldots}{N_1M_1 + N_2M_2 \ldots\ldots}$$

Weight average molecular weight can be determined by viscosity method or ultracentrifuge method. The value of weight average molecular weight is always greater than number average molecular weight.

Given – $M_A = 10{,}000$ & $M_B = 20{,}000$

Now for mixture (1) having 2A + B, we have $N_1 = 2$, $M_1 = 10,000$, $N_2 = 1$ and $M_2 = 20,000$

$$\overline{Mn} = \frac{\Sigma N_i M_i}{\Sigma N_i} = \frac{N_1 M_1 + N_2 M_2}{N_1 + N_2}$$

$$= \frac{2\times 10,000 + 1\times 20,000}{2+1} = \frac{40,000}{3}$$

$$= 13,333.4$$

$$\overline{Mw} = \frac{\Sigma N_i M_i^2}{\Sigma N_i M_i} = \frac{N_1 M_1^2 + N_2 M_2^2}{N_1 M_1 + N_2 M_2}$$

$$= \frac{2\times(10,000)^2 + 1\times(10,000)^2}{20,000 + 20,000}$$

$$= \frac{2\times 10^2 + 4\times 10^2}{40,000} = 15,000$$

Now for mixture (2) having A + 2B, we have $N_1 = 1$, $M_1 = 10,000$, $N_2 = 2$ and $M_2 = 20,000$

$$\overline{Mn} = \frac{\Sigma N_i M_i}{\Sigma N_i} = \frac{N_1 M_1 + N_2 M_2}{N_1 + N_2}$$

$$= \frac{1\times 10,000 + 2\times 20,000}{3}$$

$$= \frac{50,000}{3} = 16,333.4$$

$$\overline{Mw} = \frac{\Sigma N_i M_i^2}{\Sigma N_i M_i}$$

$$= \frac{N_1 M_1^2 + N_2^2 M_2^2}{N_1 M_1 + N_2 M_2}$$

$$= \frac{1\times(10,000)^2 + 2\times(20,000)^2}{1\times 10,000 + 2\times 20,000}$$

$$= \frac{10^8 + 8\times 10^8}{50,000}$$

$$= \frac{9\times 10^8}{5\times 10^4} = 1.8 \times 10^4$$

3. During the past few years considerable advances have been made in the development of polymeric materials for use in medicine and surgery particularly for replacements in the cardiovascular system. A number of polymers with proper surface modification which can remain biocompatible for several months are now available. Heart valves, heart-lung devices, catheters, artificial membranes, pacemaker and blood pump are devices which are made from polymeric biomaterials. The successful use of polymeric implants are improved the quality of life of many patients. But the state of art of the production of these polymeric materials for a specific perpose has not been perfected. New polymeric biomaterials are being developed to make good prostheses devices which will enable the patients without limbs to lead a normal life. The commercial polymers can not be used for biomedical applications. They do not have sufficient purity and reproductibility. The polymeric material must meet the need of the surgeons as well as the design problems of the implant. The polymeric material must meet the criteria outside and inside of a physical system. For example chemical inertness and mechanical strength are outside criteria for selection of polymer but the functional characteristics of the polymer with physiological system are inside criteria for the selection or designing the composition of a polymer.
4. **Selection of polymeric biomaterial:** Certain sets of information that case help in selection of polymeric biomaterial for making of an implant can be grouped into two categories viz (1) General characteristics and (2) Special considerations. The general characteristics which a biomedical polymer must have (1) chemical purity (2) good fabrication methodology (3) adequate mechanical strength (4) no leachable

impurity (5) easy stretchability. The presence of traces of catalyst, residual additive or other impurities in the polymeric implant may trigger thrombosis formation, protein deposition or giant cell growth or any other unfavourable tissue response. Similarly the fabrication history has great significance and biomedical polymer must retain its characteristics even after fabrication. The polymeric material of the implant is reacted upon by physiological environment. The implant must function without being itself demaged and without causing adverse effect on the tissues surrounding it. Hence polymeric biomaterial should not cause – (1) thrombosis (2) any distruction of cellular element of blood (3) cancer (4) toxic and allergic response from tissues (5) adverse effect on immune system (6) depletion of electrolytes (7) fatal effect on enzymes and proteins.

5. Specific considerations mean that a polymeric biocompatible material is designed specifically to meet the functional requirement in the prevalent environment inside the body. To accomplish this, an understanding of the relationship of the structure and properties of the polymer with respect to its interaction with physiological system at molecular level is required. The specific considerations for designing are :
   (*a*) *Type of polymers:* certain rigid and elastometric polymers evoke less tissue reaction and thrombosis formation than other.
   (*b*) *Molecular weight and Molecular weight distribution:* Most of mechanical properties of a polymer improve with molecular weight upto a limiting value and then remain constant with further increase in molecular weight. Similarly melting point, elasticity and other properties are found to have same trend. However solubility and brittleness shows reverse trend. Therefore, molecular weight of the polymers should be above the limiting value. The properties of the polymers are also affected by the molecular weight distribution of the polymers which should not be broad. Incase of broad distribution, polymer may have two molecular weight chains which may dissociate and leak into the blood stream causing malfunction.
   (*c*) *Crystallization and intermolecular forces :* Flexible polymer can be obtained by keeping the chain separated from one another otherwise the polymer will be crystalline and rigid. If crystallisation of the polymer occurs when implanted, stress cracking and stiffening of polymer take place. The highly crystalline polymers like nylon, polyethylene and polypropylene are made flexible with addition of plasticisers. However they can undergo extensive molecular rearrangement under tensile and other stresses and they may again become crystalline. Due to this, they can readily crack or develop pits. These sites also become areas for absorption of protein molecules. The presence of strong intramolecular forces fevours crystallisation of linear polymers which leads to cracks and protien absorption on the surface of the polymer.
   (*d*) *Mechanical properties:* An implant or prostheses device has a mechanical function to perform and hence its materical must have enough mechanical properties which depend upon its processing, fabrication, shape, stress and strain relationship and its time dependent changes (creep and deformation). The properties of a polymer like molecular weight and

molecular distribution and crystallinity (crystallinity can be prevented by plasticizers) can be controlled which will ensure a good performance of the polymer.

(*e*) *Surface characteristic:* The surface of a polymer which comes directly into contact with tissues and blood, plays an important role in deciding the biocompatiblity of the polymer. When blood comes in contact with the polymer, there is a rapid absorption of plasma protein on its surface. Subsequent interaction results into the absorption of platelets of the blood which leads to the thrombosis depending upon the nature of the primary layer of proteins. The absorption of proteins from the plasma depends upon the type of surface, hemorheological parameters and types of ionic species present in plasma. The nature of protein absorbed depends upon the physical and chemical nature of the surface of the polymer. Smooth surface of the polymer which is free of pits, cracks and roughness does not absorb proteins. The smoothness of the surface depends upon the micromolecular structure of the polymer and also on its surface treatment.

CERTAIN POLYMERIC BIOMATERIALS

1. **Polyvinyl chloride (PVC):** It is an amorphous and rigid polymer as it has large side group. It has a high melt viscosity which makes its processing difficult. Thermal stabilisers are added to prevent thermal degradation. Plasticizers are added to make it flexible. Lubricants are added to increase melt flow during processing. PVC is used in film form for blood bags, solution bags and surgical packaging. PVC tubing is used in catheters, cannulae dialysis devices and IV administration.
2. **Polyethylene (PE) :** It is available in many grades depending upon density as (1) high density polyethylene (HDPE) (2) low density polyethylene (LDPE) (3) very low density polyethyelene (VLDPE) (4) Linear low density polyethylene (LLDPE) (5) Ultra high molecular weight polyethylene (UHMWPE). HDPE is used for bottles, caps and non woven fabric. LDPE is used for packaging, flexible containers and nonwoven disposeables. LLDPE has excellent puncture resistance and therefore it is used for pouches and bags. Extruded tubes are made of VLDPE. UHMWPE has high density and high mechanical properties. It is used for orthopedic implant such as acetabular cup of tibia in hip joint and patellar surface in knee joint.
3. **Polypropylene (PP):** Thermal and physical properties of polypropylene are similar to polyethylene. Polypropylene has a very high flex life and high resistance to environment stress cracking. It is used for prostheses for finger joint, disposable hypothermic syringes, membrane of blood oxygenator, packaging for devices, containers (solution and drugs), suture, artificial vascular grafts and non woven fabrics etc.
4. **Polystyrene (PS):** High impact polystyrene (HIPS), PS foam and general purpose polystyrene (GPPS) are three grades available. GPPS has good transpancy, ease of fabrication, thermal stability, low density and high modulus. Its ductility, impact strength and resistance to stress cracking can be improved with addition of modifier. It is used for vacuum canisters and filterware. One of the copolymer of polystyrene is acrylonitrile butadicne - styrene (ABS) which has good surface

properties and dimensional stability. It is used for IV sets, blood dialyzers, diagnostic test kits and clamps etc.

5. **Polymethylmeth acrylate (PMMA):** It is amorphous and it has good resistance (in dilute alkalies and inorganic solution), light transparency and excellent optical properties, good weathering properties and good machineability. It is used for blood pumps and reservoirs, IV systems, membranes for blood dialyzer, contact lenses, implantable ocular lenses, dentures and bone cements for prostheses fixation etc.
6. **Polyesters :** Polyethylene terephthalate (PET) is most common polyster which is used for biomedical applications such as vascular graft, sutures and meshes. PET can also be converted by conventional techniques into moulded articles such as lucer filters, check valves and catheter housing.
7. **Polyamids (Nylons):** Nylons are designated by number of carbon atoms in the repeating units. For example Nylon 6 and Nylon 11. The presence of CONH groups provides attraction between chains and improves physical properties such as strength. Certain nylons have specific strength which is five times that of steel and they are most suitable for composites. However nylon is hygroscopic and they lose strength in vivo when implanted.

APPLICATION OF POLYMERS

1. The applications of polymers as biomaterials have been elaborated with each type of polymer. However some other applications are :

S.N.	Polymer	Application
1.	Segmented polyurethane	Artificial heart, heart valves, vascular tubing
2.	Polyalkyle siloxane	Heart valve, hydrocephalus drain link
3.	Segmented copolydimethyle siboxane urethane	Heart valve
4.	Perfluoro butynyl ethyle cellulose	Membrane of oxygenator
5.	Polyalkyle sulfone	Membrane of oxygenator
6.	Hydrogels	As grafted surface for polymers having good mechanical properties
7.	Silicon rubber with silica filler and coated with free silicon	Cosmetic space filler.