A Polymer Used in the Novel Drug Delivery System

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***Abstract*- Polymer used in becoming novel drug delivery system. The main role of polymer is to protect drug from physiological environment and prolong release of drug to improve its stability. The drug is release from polymer by diffusion, degradation and swelling. Several polymer are used to investigated in novel drug delivery system such as, Polymeric hydrogel, microencapsulation, adhesive biomaterial, nanoparticle, polymeric implant, polymeric micelles, liposome, ethosomes, polmer in therapeutic gene therapy. Drug delivery is a concept heavily integrated with dosage form and route of administration. The aim for new drug delivery system is controlled delivery to make ideal drug, selective targeting to the site of action. Polymer are tools used in novel drug delivery system to modify the drug release of pharmaceutical dosage form polyox.(polyethylene oxide) multifunctional polymer used in novel drug delivery system.**

***Index terms*- Adhesive Biomaterial, Polymeric Hydrogels, Polymeric Micelles, Novel Drug Delivery System.**

INTRODUCTION

Polymer is compound high molecular masses are formed. Polymer is very large molecules made hundreds of monomers join to form long chain. The word polymer comes from the Greek words poly means many and mer means parts. Polymer is used as a synonym for plastic. All plastics are polymers but not all polymers are plastics.

Organic polymer play crucial role in living things, providing basic structural materials and participating in vital life processes. For example, the solid parts of all plant are made up of polymer…. Starches, important sources of food energy derived from plants are natural polymer composed of glucose. 3.1 polymer sources of synthetic polymer. The most important primary sources of synthetic polymer are crude oil, natural gas and to minor extent, coal. Because all are primarily fuel rather than sources of materials, the manufacture of polymer is susceptible to changes in prices or supply. When monomers join with other monomers through the process of creating covalent bonds, they form larger molecules, called polymers. If it bonds with three or more molecules then three dimensional, cross linked structures can form (Source: Innovate Us). Polymers can occur naturally, or we can manufacture them.

Polymer is used extensively in our daily routine life. The earliest drug delivery system introduced in 1970s was based on polymer formed from lactic acid.

Advantage of polymeric drug delivery products are as follows:

1. Stabilization of the drug: The polymer can protect the drug from the physiological environment and hence improve its stability in vivo.
2. Localized delivery of drug: The product can be implanted directly at the site where drug action is needed and hence systemic exposure of the drug can be reduced.
3. Sustained delivery of drug: The drug encapsulated is released over extended periods and

Novel drug delivery system are various prodrug such as transdermal drug delivery systems, ocusert ,insulin

jet and micro pump controlled delivery system patient controlled analgesia (PCA) , drug eluting stents, gene therapy. Novel drug delivery system is to provide a therapeutic amount of drug to the appropriate site in the body to accomplish promptly and then maintain the desired drug concentration. To minimize drug degradation and loss. To increase bioavailability of the drug absorbed in the required site.

COMMON TERMINOLOGY USED IN NDDS

1. Controlled action

Dosage forms with controlled action provide a prolonged duration of drug release with predictability and reproducibility in drug release kinetics i.e. the drug is released in a controlled fashion.

2. Sustained action

Dosage forms with sustained action, initially release a sufficient amount of drug to produce a desired pharmacological effect and then release the remaining fraction of drug periodically to prolong their presence in systemic circulation and sustain their duration of action

Polymers used for novel drug delivery

1. Polymeric hydrogels :

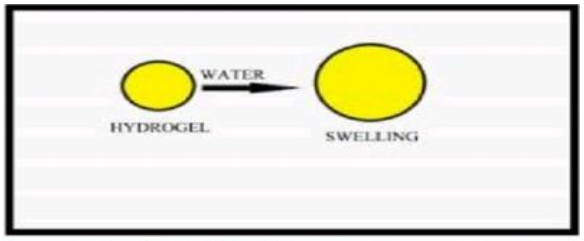


Fig. polymeric hydrogel drug delivery system.

Three dimensional networks of hydrophilic polymer chain that do not dissolve can swell in water. High bio compatibility. Environmental stimuli respondent: 1. Temperature 2. PH 3. Light. High water content capacity. Hydrogels contains interactive functional groups attached to the main polymeric chain are usually referred to as smart hydrogels.

2. Hydrogels in drug delivery:

Drug can be loaded into hydrogels in two ways. First, drug, initiator and cross linker can be mixed and subsequently polymerized to confine the drug with in matrix. Alternatively, a preformed hydrogels can be allowed to swell equilibrium in a suitable drug solution.

3. Release mechanism:

- Diffusion
- Osmosis
- Ion exchange

4. Various applications of hydrogels:

Moisture trap. Disposable diapers or sanitary towels, Controlled release drug delivery. Gastric retention device, Would dressing. Hydrogels modified fabrics for cosmetic or pharmaceuticals. Per oral peptide delivery system (drugs).Topical drug delivery. Soil moisture maintenance.

5. Hydrogels as drug delivery system pros and cons:

ADVANTAGES:

The main advantage of hydrogels is that they process a degree if flexibility very similar to natural tissue, due to their significant water content. They are biocompatible, biodegradable and can be injected. Hydrogels also possess good transport properties and easy to modify.

LIMITATION:

The lack of specific cell adhesive properties of PEG hydrogels as scaffold for tissue engineering. Low mechanical strength of calcium alginate hydrogels. The lack of efficiency and suitability as carriers for small molecular weight and hydrophobic active pharmaceutical. Rapid drug release and low drug loading.

6. Microencapsulation:

It is the process by which very tiny droplets or particles of liquid or solid material are surrounded or coated with continuous film of polymeric material. They made by,

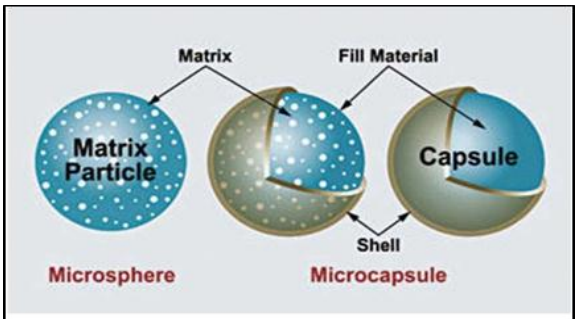


FIGURE 2. Different micro-particle structures

interracial polycondensation:1. Polymer forms at boundary of two phases. 2. Proteins and cells can be encapsulated. Controlled gelatin in aqueous solution.

Eg. Addition of sodium alginate +drug in water. Polymer capsules containing active therapeutic: natural or synthetic polymer can be used to form capsules.

7. Mode of drug release for NDDS

- Physical disruption of capsules.
- Diffusion through porous capsule membrane.
- Role of polymers are substances of high molecular weight made up by repeating monomer unit.

8. Adhesive biomaterials :

Bio adhesive are natural or synthetic materials, that can attach to the biological surfaces and be retained therefore an extended period of time. These drug delivery systems exhibits superior contact, improved adhesion, prolonged residence time, and hence enhanced absorption at a selected application site. Such polymer are sometimes referred to as biological glues because they are incorporated into drug to enable the drugs to bind to their target tissue.

9. Examples of bio adhesive polymer

a. Acacia gum: This natural polymer is a dried gum obtained from the stem and branches of the tree. Acacia Senegal, it is used as thickener in pharmaceuticals.
b. Alginic acid: It is a natural polymer found in cell wall of brown algae .it is widely used in the manufacturing of alginate salts such as sodium alginate.
c. Carbomers: They are poly acrylic acid polymer. They are widely used in the pharmaceutical and cosmetic industries as thickening agents.
d. Hydroxy propyl methyl cellulose (HPMC):This polymer is included in preparation used to moisten contact lenses and in oral gels.
e. Sodium hyaluronate: A high molecular weight polymers. This polymer is used during intraocular surgery to protect cornea and also acts as a tear substitute in the treatment of dry eyes.

Other examples of polymer include such as pectin, polyvinyl alcohol, polyvinyl pyrrolidone (PVP) tragacanth, chitosan.

10. Bioadhesive Drug delivery system:

In bioadhesive drug delivery system this term bioadhesive is used to describe the bonding or adhesion between a synthetic or natural polymer and soft tissue such as

11. Targets for bioadhesive formulations:

Bioadhesive or mucoadhesive formulation has been targeted to various anatomical locations to aid drug delivery and absorption. Drug delivery to each anatomical region is displayed in below table.

Sr. No.	Body site	System
1	Eye	Mucoadhesive eyedrops/inserts.
2	Nasal cavity	Nasal drug delivery system.
3	Oral cavity	Dental gel/buccal cavity.
4	Skin	Patches, tapes, dressing.
5	Vagina	Local vaginal delivery system.
6	Rectum	Local/systemic rectal delivery systems.

12. Novel mucoadhesive polymer:

In novel mucoadhesive polymer cases, existing mucoadhesive polymer have been modified while in other, new material are developed.

a. Lectin: According to the molecular structure, three groups of pectin can be distinguished.
    - Merolectin: lectin having only one carbohydrate recognizing domain.
    - Hololectin: lectin with two or more carbohydrate recognizing domain.
    - Chimerolectin: lectin with additional unrelated domain.
b. Thiolated polymers.
c. Bioadhesive nanopolymer as drug carriers.
d. Alginate polyethylene glycol acrylate (alginate – PEGAc).
e. Poloxome.
f. Pluronics and combination.
g. Other novel mucoadhesive polymers.
h. Bacterial adhesions.
i. Amino acid sequence.
j. Antibodies.

13. Nanoparticles:

In nanoparticles novel drug delivery system, the drug is incorporated into a suitable oriented particle system and delivers the drug toward its site of action in the body and improve its cellular interaction. Nanoparticles varying in size 10 to 1000nm.

Nanoparticles based drug delivery: Using nanotechnology the drug can be targeted to a precise location which would make the drug much more effective and reduce the chances of possible side effects. More specific drug delivery targeting delivery. Reduction in toxicity while maintaining therapeutic efficiency.

Achievement 1.Once daily oral ciprofloxacin. 2. Tumor targeted delivery. 3. Improved ophthalmic delivery. 4. Oral insulin.5.oral administration of other peptides.

The drug is dissolved, entrapped, encapsulated or attached to a matrix. The rate of drug release from the nanoparticle and subsequent polymer degradation are important parameters for a successful formulation. The rate of drug release depends upon the,

- Properties of the nanoparticle polymer.
- Method of drug loading into the nanoparticle

14. Polymers in Implants

This drug delivery system is to use hydrolytically labile polymers into which a drug could be physically dispersed under mild conditions and drug release controlled by hydrolytic erosion of the polymer matrix over a period of time with a simultaneous or subsequent degradation of polymer in the tissue. Implant can be prefabricated and administered with the help of specialized injection devices such as trocars, often under local anesthesia.

15. Manufacture of implant:

- Hot melt extrusion.
- Compressing polymer and drug mixture.
- Injection molding to yield different sizes and shapes (flats film, rolled implants rods,etc.).

16. ATRIGEL: This approach was adapted by Atrix Laboratories indeveloping proprietary technology called Atrigel .The discomfort associated with implantation procedure can be alleviated by use of in situ forming implants that are formed at the site of injection on injecting a polymeric solution.

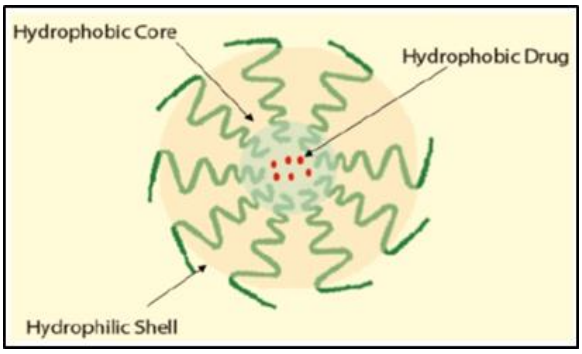
17. Polymeric Micelles:

Polymeric micelles are used as drug carriers. These drug carriers are mostly used for the targeting hydrophobic drugs. Polymeric Micelles is a macro molecular assembly that forms block co polymers or graft polymers, and has a spherical inner core and an outer shell. In micellar structure, one segment of the block copolymer can provide enough interaction cohesive interactions. The cohesive interactions in polymeric,

a) Hydrophobic interaction:

Most of the drug molecules possess a hydrophobic character, hydrophobic interaction are used most commonly for drug targeting.

b) Electrostatic interaction:



The electrostatic interaction may be applied to macromolecules with electric charges at a high density. Eg DNA and RNA proteins with a large number of charged groups (aspartic acid, lysine).

c) Hydrogen bonding and pi – pi interaction:

These may work cooperatively with other cohesive interactions. E.g. drugs with aromatic rings.

The drug can be incorporated into a polymeric micelle by 2 methods such as 1.

1. Chemical conjugation
2. Physical entrapment.

The purpose of the incorporation of drugs into polymeric Micelles, Drug targeting, Controlled or sustained release of drug, Solubilization of drug.

Examples of drug targeting with polymeric Micelles carriers:

Drug	Polymeric carriers	Uses
Doxarubicin	PEG poly (aspartic acid) block copolymers.	Anticancer
Cisplatin	PeG poly (aspartic acid) block copolymers activity.	Anti tumor
Taxol	PEG PLA based polymeric Micelles	Anticancer
Amphotericine	PEG poly (N hexyl aspartamide) block copolymers.	Systemic fungal infection

Drug delivery system based on polymeric Micelles and Ultrasound:

Some of the most common drugs used in chemotherapy belongs to the anthracryline family, and Doxarubicin (Dox) is widely used with high efficiency against several cancer.

The literature suggests the importance of determining the micellar stability in order to know if their structure can release and re encapsulate the once the Michelle's reach the intend site.

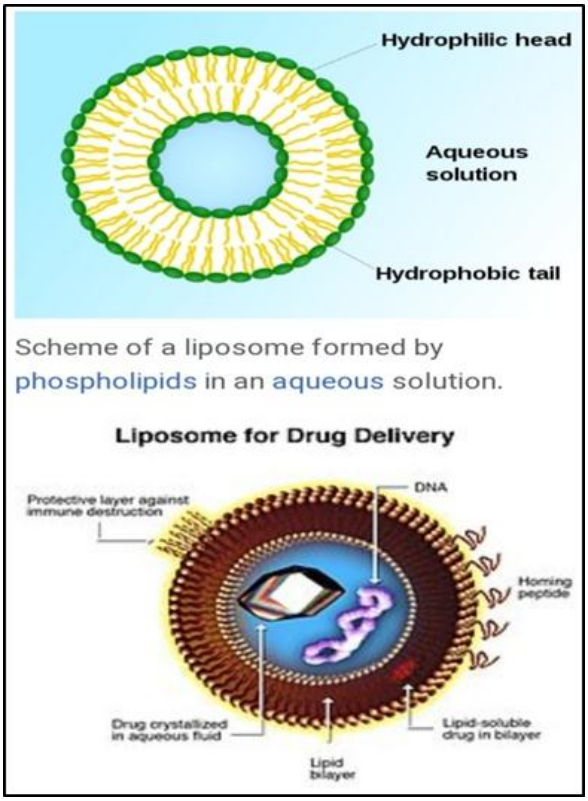
POLYMERS IN THERAPEUTIC GENE THERAPY

- Gene therapy: The genetic material is transferred into patient so that the resulting circumvention of genetic abnormalities can bring out therapeutic effects in the patient.
- Targeted polymeric gene carriers: There are numerous targeting ligands that can be utilized for cell specific gene transfer, including asialo glycoprotein, lactose, low density lipoproteins (LDL), folic acid, and antibodies, so on.

Some of the cationic graft copolymers:

a. Poly (L- lysine)-PLL.
b. Poly (N- hydroxy propyl methoacrylamide) – HPMC.
c. Poly ethylene imine- PEI.
d. Poly (2-dimetyl amino) ethyl methacrylate – p – DMAEMA.

LIPOSOMES



The first discovered in 1965 and proposed as drug carriers afterwards. Microscopic vesicles formed when an aqueous suspension of phospholipid is exposed to ultrasonic agitation. Large multilayered vesicles or small signal layered vesicles or small single layered vesicles may be formed. The clinical potential of liposome of as vehicle for replacement therapy in genetic deficiencies of lysosomal enzymes was first established in 1970s (4,5) Considerable progress was made during 1970s and 1980s in the field of liposome stability leading to long circulation time of liposome after intravenous administration resulting in the improvement bio- distribution of liposomes.

ATTRACTIVE BIOLOGICAL PROPERTIES OF LIPOSOMES:

Liposomes are biocompatible. Liposomes can entrap water soluble (hydrophilic) pharmaceutical agents in their internal water compartment and water - insoluble (hydrophobic) pharmaceuticals into the membrane.

ADVANTAGE

Provide controlled drug delivery .Biodegradable, biocompatible, flexible. Non-ionic. Can carry both water and lipid soluble drugs. Improve protein stabilization. Controlled hydration. Act as reservoir of drugs.

POLYMERS IN TISSUE ENGINEERING:

Tissue engineering is to employ the novel biomaterials to facilitate the regeneration or replacement of damaged tissue or diseased tissue.

Advances in recombinant techniques have led to the development of genetically engineered polymers with exquisite control over monomer sequence and polymer length.

Genetic engineering methodology offers the ability to synthesize protein based polymers with precisely controlled structure

Genetic engineering methodology has enabled the synthesis of protein- based polymers with precisely controlled and structures. Protein- based polymers have well defined molecular weight, monomer composition sequences and steriochemistries.

CONCLUSION

Polymers are the technology of prolonged release drug formulations macromolecules has also found the application in the technology of prolonged release drug formulations. The pharmaceutical technology is one of the most important fields of using of polymers. The utilized compound is primarily friendly for environment safe nontoxic and

irreplaceable for the synthesis of polymers for the pharmaceutical applications. At the time of delivery, it is obvious that the possibilities for delivery of diagnostic and therapeutic agents using polymer Micelles are extremely broad and one should expect further increases in the laboratory .Polymers have a low density they can be used in electrical insulation and they also swell with water require low temperature and have a sensitivity to uv light. Polymer is easily to produce and cost effective, but many are inflammable and have certain toxicity. They cannot with stand very high temperature as all plastics melt down very soon as compared to metals. The strength to size ration of polymer is less while for metal is more. The toxicity was mainly caused by fat soluble organic substances. The elaboration of new medical and, pharmaceutical specimens will also require intensive investigations in chemistry and biomedical polymer areas.

REFERENCES

[1] https: //www .Britannia. Com> science (polymer importance).
[2] Introduction to polymer 3.1 primary sources of synthetic polymers. https://www.open.edu>chemistry.
[3] Problem with polymer, https://coggle. It (diagram) problem.
[4] Give advantage and disadvantage of polymers, https://www.ques10.com.
[5] Polymer stuff works science, https://www.science how stuff works .com.
[6] plastic products leach toxic substances phys. Org, https://m.phys.org>new>2011- 0.
[7] Polymers used in the designing of controlled drug delivery system, www. Rjptonlindisadva
[8] Polymer used in novel drug delivery system, https://www.scribd.com.
[9] Surya amol, novel drug delivery system, https: //www.slideshare.net>
[10] Jain NK; controlled and novel drug delivery; CBS ppublication.
[11] Paris Ghasemiyesh, soliman Mohammad;- samani., Hydrogels as drug delivery system; Pros and Cons.
[12] Garima singh, alka kahani,shiv Shankar Bhatacharya.(journal of fundamental research).,Hydrogels as novel drug delivery system : review.
[13] K.M. Manjana, B shivakumar, and T.M. pramod Kumar (microencapsulation : An Acclaimed Novel drug delivery system for NSAIDS Arthritis.).
[14] Mythri .G, K. Kavitha, M. Rupesh Kumar, sd. Sagadesh singh. (Journal of applied pharmaceutical science). Novel mucoadhesive polymers.
[15] Rafeeq Tambour, Ana. M. Martins, William G. Pitt and Ghaleb A. Hosseini., Drug delivery system based on polymeric Micelles and Ultrasound: A review.
[16] Navneet kumar verma and Asha Roshan., A Review – A targeted Drug Delivery system.
[17] Jordant Frandsen at al. Chem Soc Rev, 2012, Recombinant protein based polymers for Advanced Drug Delivery.
[18] A Nagarsekar et al.J Drug Target. 1999, Genetically Engineered polymers for Drug Delivery (Review).
[19] Mohamed Haider et al. 5 Control Release, 2004, genetically engineered polymers status and prospects for Controlled Release.
[20] Global research online.net.
[21] https://www.quora.com>.