IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 2, October 2024

Preparation of Polymeric Nanoparticles : An Overview on Polymers

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Abstract: *The polymers used in pharmaceutical medication delivery of therapeutic agents are the subject of the current review study. Tablets, patches, cassettes, films, semisolids, and powders are some of these dose forms. Because they regulate the medication's release from the device, polymers are the fundamental component of pharmaceutical drug delivery systems. Because biodegradable polymers can be broken down to biodegradable polymer-based medication release can be produced at a consistent rate, with non-toxic monomers, gadget for controlled release. Predefined medication delivery rates can be attained by using natural polymers, and their Its physico-chemical properties and accessibility offer a basis for its application as a polymer in drug delivery systems. Because of their well-established biocompatibility and biodegradability, biodegradable polymers have found extensive application in the biomedical field. Polymers are typically employed as implants in the biomedical field, where they are supposed to provide long-term functionality. These advancements help to reduce adverse effects and various forms of side effects while also increasing the effectiveness of medical treatment. difficulties for the sufferers. The major job of polymer is to shield drug from physiological environment and prolong release of drug in order to increase stability. Through swelling, breakdown, and diffusion, the medication is released from the polymer. Furthermore, this study additionally provides properties and behaviors of mucoadhesive polymers produced from plants that are now utilized in medication delivery. Polymeric nanoparticles (NPs) are particles within the size range from 1 to 1000 nm and can be loaded with active compounds entrapped within or surface-adsorbed onto the polymeric core. The term "nanoparticle" stands for both nanocapsules and nanospheres, which are distinguished by the morphological structure. Polymeric NPs have shown great potential for targeted delivery of drugs for the treatment of several diseases.*

Keywords: polymerization, P'ceutical application , polymeric nanoparticles, preparation methods, Application

I. INTRODUCTION

Pharmaceutical polymers, which provide several benefits such better drug solubility, controlled release, and increased bioavailability, are essential to the development and formulation of different drug delivery systems. Pharmaceutical polymers need to meet specific physical and chemical requirements for their intended use, as well as being non-toxic and biocompatible. A polymer is a material or substance made up of numerous big molecules, often known as macromolecules repeated sections. Because of their wide range of characteristics, both natural and manmade polymers play crucial and roles that are commonplace in daily life. Natural polymers and well-known manmade plastics like polystyrene are examples of polymers. Biopolymers, which are essential to biological structure and function, include proteins and DNA [1]. Polymers, Both natural and artificial materials are produced by polymerizing several tiny molecules known as monomer. A broad range of materials known as pharmaceutical polymers are employed in many pharmaceutical applications.

They can be applied to regulate medication release, enhance drug stability, and distribute pharmaceuticals to certain bodily locations. Nowadays, polymers are employed in many different medicinal applications, such as:

medication delivery systems: Polymers are used to generate a range of medication delivery systems, including tablets, capsules, injectables, implants, transdermal drug delivery methods, and topical preparations.

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Excipients: Polymers are also employed as excipients in a range of medicinal compositions. The excipients don't work. components that are used in formulations to enhance their stability, processing, or delivery qualities.
Medical equipment: Stents, catheters, artificial organs and other devices that are employed in the treatment of patients are made of polymers. [1,2]

II. POLYMERIZATION

Small molecules known as monomers are chemically bound to one another during the polymerization process to create the long-chain or three-dimensional network structure known as a polymer. Many synthetic polymers, plastics, and numerous natural materials are produced via this technique, which is essential. Polymerization can take place by distinct mechanisms and in diverse circumstances.[3]

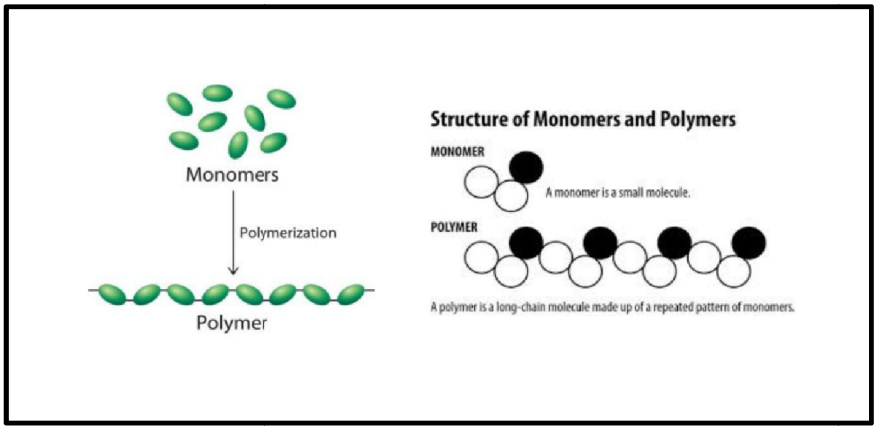

Fig-1. Process of polymerization

III. CLASSIFICATION OF POLYMERS

3.1. Basis on interaction with water

- Non-biodegradable hydrophobic Polymers:- E.g. Polyvinyl chloride,
- Soluble Polymers:- E.g. HPMC, PEG
- Hydro gels:- E.g. Polyvinyl pyrrolidine

3.2. Based on polymerisation method

- Addition Polymers:- E.g. Alkane Polymers
- Condensation polymers:- E.g. Polystyrene and Polyamide

3.3. Based on polymerization mechanism

- Chain Polymerization
- Step growth Polymerization

3.4. Based on chemical structure

- Activated C-C Polymer
- Inorganic polymers
- Natural polymers

3.5. Based on occurrence

- Natural polymers:- E.g. Proteins, collagen, keratin, albumin, cellulose
- Synthetic polymers:- E.g. Polyesters, polyamides

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3.6. Based on bio-stability

- Bio-degradable
- Non Bio-degradable

Ideal properties of polymer:

- It should be adaptable and have a broad variety of mechanical, physical, and chemical properties.
- It must possess strong mechanical properties and be non-toxic.strength and ought to be given without difficulty.
- It need to be reasonably priced and simple to make.
- It must be compatible and inert to host tissue in relation to surroundings.

Selection criteria for polymers

- The polymer ought to be soluble and simple to synthesized.
- Its molecular weight ought to be finite.
- It ought to align with biological setting.
- Ideally, it is biodegradable.
- Good polymer drug linkage should be provided.

IV. PHARMACEUTICAL POLYMERS IN THE DIVERSE DRUG DELIVERY

Pharmaceutical polymers play a critical role in diverse drug delivery systems, offering a wide range of advantages in terms of drug solubility, stability, controlled release, and targeted delivery . The diverse drug delivery systems where pharmaceutical polymers are prominently used:

4.1. Oral Drug Delivery

- Polymeric Nanoparticles and Microparticles: These can protect drugs from degradation in the gastrointestinal tract and enable controlled release.
- Polymeric Coatings: Coatings can modify drug release profiles or provide taste masking for oral dosage forms.

4.2 Injectable Drug Delivery:

- Polymeric Microspheres: Injectable microspheres enable sustained release of drugs over extended periods. Polymers like PLGA are commonly used.
- Hydrogels: Injectable hydrogels are used for local drug delivery, tissue engineering, and sustained release of biologics.[7,8,9]

4.3 Transdermal and Topical Drug Delivery:

- Polymer Matrix Patches: These patches use polymers to control the release of drugs through the skin over time.
- Polymeric Nanocarriers: Nanoparticles and liposomes can encapsulate drugs for enhanced skin penetration and targeted delivery.

4.4 Ocular Drug Delivery:

- Polymeric Nanoparticles: Nanoparticles can enhance the solubility of poorly water-soluble drugs and improve drug retention in the eye.
- Contact Lenses: Polymers are used in contact lens materials to release drugs directly onto the ocular surface.

4.5 Intravenous Drug Delivery:

- Polymeric Micelles: These can improve the solubility of hydrophobic drugs and enhance their circulation time in the bloodstream.

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- Polymeric Drug Conjugates: Polymers can be conjugated to drugs to increase their stability and reduce side effects.

4.6.Pulmonary Drug Delivery:

- Polymeric Nanoparticles: Nanoparticles can be engineered for inhalation delivery, allowing targeted treatment of lung diseases.
- Polymeric Nanofibers: Nanofiber-based systems can improve drug dispersion and adhesion in the respiratory tract.

4.7.Intranasal Drug Delivery:

- Polymeric Nanoparticles: Nasal delivery systems use polymers to encapsulate drugs and enhance their absorption through the nasal mucosa.[8,9,10,11]
- The medical and drug delivery applications of polymers as biodegradable in drug delivery system.

4.8. Gastrointestinal Drug Delivery:

- Enteric Coatings: Polymers like Eudragit are used for enteric coatings to protect drugs from stomach acid and deliver them to the intestines.
- Polymeric Microsponges: These can encapsulate drugs and release them slowly in the GI tract.

4.9. Implantable Drug Delivery Systems:

- Biodegradable Polymers: Implants made from biodegradable polymers gradually release drugs over time, eliminating the need for repeated dosing.

4.10. Targeted Drug Delivery:

- Polymeric Nanocarriers: Nanoparticles can be functionalized with ligands to target specific cells or tissues, reducing systemic side effects.

4.11. Intratumoral Drug Delivery:

- Polymeric Microspheres: Microspheres can be injected directly into tumors to provide sustained drug release at the site of action .[10,11,12]

V. LABORATORY SCALE PREPARATION OF POLYMERIC NANOPARTICLES

The laboratory-scale Nanoparticles preparation methods can be classified into two broad categories:
(1) dispersion of preformed polymers.
(2) polymerization of monomers.
The dispersion of preformed polymers methods include:
Solvent evaporation method
Solvent diffusion /emulsification method
Reverse salting out/emulsion diffusion method
Nonaqueous phase separation/nanoprecipitation methods

5.1. Solvent Evaporation method:

Materials Needed:

Polymer: Common choices include PLGA, PLA, or PCL.

1. Solvent: An organic solvent like dichloromethane (DCM) or acetone.
2. Surfactant: Optional, but can help stabilize the nanoparticles (e.g., polyvinyl alcohol).
3. Water: For the aqueous phase.
4. Sonicator: For emulsification.

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Rotary evaporator: For solvent removal.
Centrifuge: For purification.

Procedure:

1. Dissolve the polymer in an organic solvent (e.g., DCM) at a specific concentration (typically 1-10% w/v) under stirring until completely dissolved.
2. Prepare an aqueous solution containing the surfactant if used. The surfactant concentration can vary (1-5% w/v) based on the polymer and desired nanoparticle size.
3. Slowly add the organic polymer solution to the aqueous phase while stirring vigorously (using a magnetic stirrer or a homogenizer) to form a water-in-oil (W/O) emulsion.
4. For better dispersion, use a sonicator briefly (10-30 seconds) to break down large droplets.
5. Transfer the emulsion to a rotary evaporator set at low pressure to remove the organic solvent. This should be done at a controlled temperature (around 30-50°C) to prevent overheating.
6. Continue the evaporation process until the organic solvent is completely removed, leading to nanoparticle formation.
7. After solvent evaporation, centrifuge the nanoparticle suspension at high speed (e.g., 10,000–15,000 rpm) to separate the nanoparticles from the aqueous phase.
8. Discard the supernatant and re-suspend the nanoparticles in fresh water or a suitable buffer.
9. Wash the nanoparticles by repeating the centrifugation and re-suspension steps several times to remove any residual surfactant and unencapsulated materials.

Storage:

Store the nanoparticles in suitable conditions (usually at 4°C) for further use or analysis.[13,14]

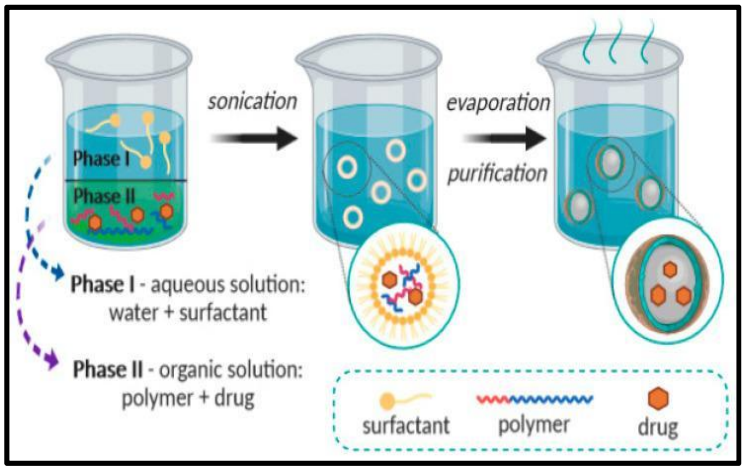

Fig-2. Solvent evaporation method for polymeric nanoparticles

5.2. Solvent Diffusion

Materials Needed

- Polymer: Choose a biodegradable polymer (e.g., PLGA, PCL).
- Solvent: A volatile organic solvent (e.g., dichloromethane, acetone).
- Aqueous phase: Typically, this is a stabilizing agent like PVA or surfactants,Distilled water.
- Equipment: Magnetic stirrer, rotary evaporator, sonicator (if necessary), centrifuge.

Procedure

1. Dissolve the chosen polymer in an organic solvent to create a concentrated solution (e.g., 1-10% w/v).Stir the solution at room temperature until the polymer is completely dissolved.

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2. Prepare an aqueous solution containing a stabilizing agent (e.g., PVA, surfactant) at a suitable concentration (typically 0.5-5% w/v).Stir the aqueous solution continuously.
3. Slowly add the organic polymer solution to the aqueous phase under continuous stirring.Use a high-shear mixer or sonicator briefly to create an emulsion (oil-in-water). Ensure that the dispersion is uniform.
4. Allow the emulsion to stir for a specified period (e.g., 1-3 hours) at room temperature. This allows the organic solvent to diffuse into the aqueous phase, leading to nanoparticle formation. Optionally, you can add a non-solvent (e.g., water) gradually to enhance the diffusion process.
5. Transfer the emulsion to a rotary evaporator to remove the organic solvent under reduced pressure. Maintain a temperature that is safe for the polymer, typically around 30-40°C.
6. Centrifuge the resultant dispersion to separate the nanoparticles from the supernatant. Wash the nanoparticles with distilled water to remove excess stabilizer and unencapsulated materials.[15,16]

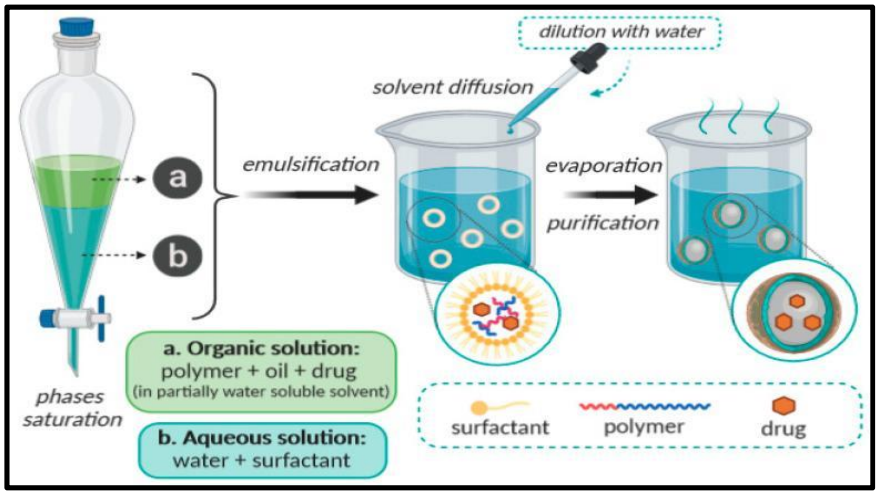

Fig-3. Solvent diffusion method for polymeric nanoparticles

5.3. Emulsification/Reverse Salting-Out

Materials Needed

- Polymer: Choose your polymer (e.g., PLGA, polystyrene)
- Solvent: Organic solvent (e.g., acetone, ethanol)
- Salting agent: Typically, ammonium sulfate or sodium chloride
- Surfactant: (optional) to stabilize the nanoparticles Deionized water
- Equipment: Magnetic stirrer, centrifuge, rotary evaporator, ultrasonic bath, and a filtration system

Procedure

1. Dissolve the selected polymer in an organic solvent to create a homogeneous solution. The concentration typically ranges from 1-10% (w/v), depending on the polymer.
2. Prepare a saturated saline solution by dissolving the salting agent (e.g., ammonium sulfate) in deionized water. Heat may be required to fully dissolve the salt.
3. Slowly add the salting solution to the polymer solution while stirring continuously. This addition should be done gradually to allow the polymer to precipitate out of the solution, forming nanoparticles.
4. Continue stirring the mixture for several hours (usually 2-4 hours) to ensure complete precipitation and uniformity of the nanoparticle size.
5. After stirring, centrifuge the mixture at a suitable speed (e.g., 10,000-15,000 rpm) for 10-30 minutes to separate the nanoparticles from the supernatant.

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6. Carefully remove the supernatant and wash the pellet of nanoparticles with deionized water or a suitable buffer to remove excess salt and unreacted materials. Repeat this washing step 2-3 times.
7. Resuspend the washed nanoparticles in an appropriate buffer or solvent for further characterization or application.[17,18]

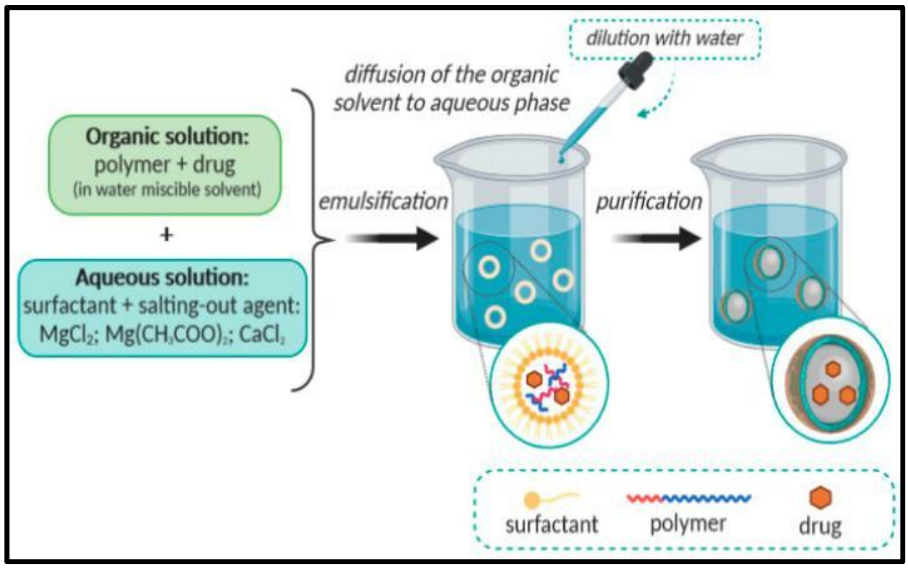

Fig-4.Reverse salting out method for polymeric nanoparticles

5.4. Nanoprecipitation

Materials Needed

- Polymer: Choose a suitable biodegradable polymer (e.g., PLGA, PLA, PCL).
- Solvent: Select a volatile organic solvent (e.g., acetone, dichloromethane).
- Non-Solvent: Use an aqueous phase (e.g., distilled water or buffer).
- Stabilizers: Optional, such as surfactants or polymers (e.g., PVA, Tween).
- Equipment: Magnetic stirrer, syringe, needle, and optionally a high-speed homogenizer or Preparesonicator.

Procedure

1. Determine the desired amount of polymer based on your formulation.
2. Dissolve the polymer in an appropriate solvent. Use a concentration typically between 1% and 10% (w/v).
3. Stir the solution at room temperature until the polymer is comvpletely dissolved.
4. Measure the required volume of distilled water or buffer in a separate container.
5. If using stabilizers, dissolve them in the aqueous phase.
6. Using a syringe, inject the polymer solution into the non-solvent phase rapidly. This should be done under continuous stirring to ensure uniform mixing.
7. A fast injection rate promotes the formation of smaller nanoparticles.
8. Continue stirring for a specified time (typically 30 minutes to 1 hour) to allow nanoparticles to form and stabilize.
9. After sufficient stirring, centrifuge the mixture at a suitable speed (e.g., 10,000-15,000 rpm) for 10-30 minutes to pellet the nanoparticles.
10. Carefully remove the supernatant to isolate the nanoparticles.
11. Resuspend the pellet in fresh non-solvent or buffer and centrifuge again to remove any unencapsulated polymer or surfactant.
12. This washing step can be repeated 1-2 times to ensure purity.
13. Resuspend the washed nanoparticles in a suitable buffer or solvent for storage or further use.[19,20]

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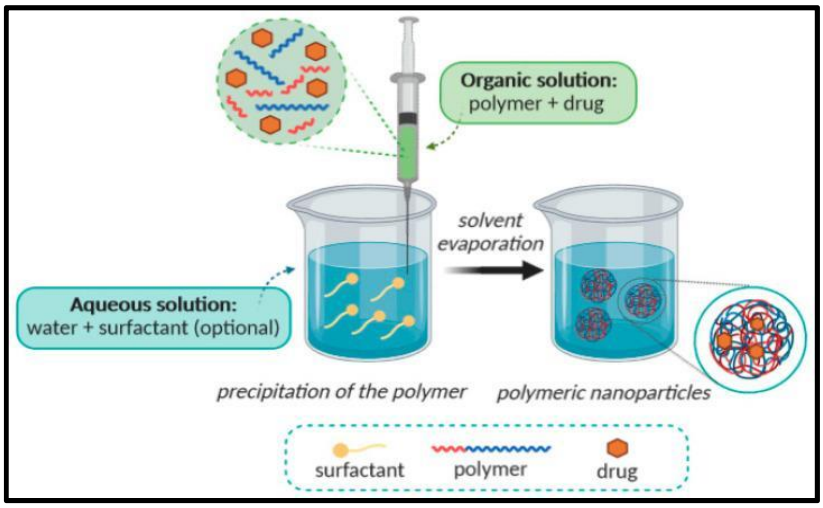

Fig-5. Nanoprecipitation method for polymeric nanoparticles

VI. APPLICATION OF POLYMERIC NANOPARTICLES

1. Drug Delivery

- **Targeted Therapy:** Polymeric nanoparticles can be designed to deliver drugs specifically to targeted tissues or cells, minimizing side effects and enhancing therapeutic efficacy.
- **Controlled Release:** They allow for the controlled release of drugs over time, which can improve the duration of action and patient compliance.

2. Biomedical Applications

- **Imaging Agents:** Used as contrast agents in medical imaging, improving the visualization of tissues and tumors.
- **Gene Delivery**: Capable of delivering genetic material (DNA/RNA) to cells for gene therapy, offering potential treatments for genetic disorders.

3. Vaccines

- Polymeric nanoparticles can serve as adjuvants or carriers for vaccines, enhancing immune response and stability.

4. Diagnostics

- Used in biosensors and diagnostic assays to improve the sensitivity and specificity of detecting biomarkers or pathogens.

5. Environmental Applications

- Used for the removal of pollutants from water and air, as well as in waste management through encapsulation and degradation of harmful substances.

6. Cosmetics and Personal Care

- Incorporated in formulations for sustained release of active ingredients, improving efficacy and stability in skincare products.

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7. Agriculture

- Used in the formulation of pesticides and fertilizers for targeted delivery and controlled release, enhancing effectiveness and reducing environmental impact.

8. Food Industry

- Employed in food packaging to improve shelf life and reduce spoilage by controlling the release of preservatives.
- These diverse applications highlight the versatility of polymeric nanoparticles in advancing technology and improving health outcomes across various sectors.

VII. CONCLUSION

Polymers are crucial components in the pharmaceutical sector, to sum up. They have a wide range of uses and are essential to enhancing the ease, safety, and effectiveness of drug administration. Additionally, polymers are being utilized to create biomaterials and novel medication delivery methods. The review paper has illuminated the diverse and essential function of polymers in the pharmaceutical industry. Drug formulation, distribution, and a host of other medicinal uses have all been transformed by polymers. Innovative drug delivery methods that target specific body areas, offer regulated and prolonged drug release, and improve the bioavailability of poorly soluble medications have all been made possible by them. Additionally, polymers have added to the solubility and stability. Polymeric Nanoparticles are very important in medical field. It also important in Various industries ie. Biotechnological, pharmaceutical, etc. It used in various drug delivery systems.

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