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Review Article

Review on Polymeric Nanoparticle

Review on Classification, Methods, and Characterization of Polymeric Nanoparticles with Their Applications

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Abstract: The majority of this review's emphasis is given to polymer-based nanoparticles, including their production, evaluation and their bioavailability. Biodegradable and biocompatible polymers of synthetic and natural origin make up the matrix of polymer-based nanoparticles. By reducing the size of the particles, polymer-based nanoparticles can significantly improve the solubility of poorly water-soluble drugs. Polymeric nanoparticles are excellent for directing a drug's action at a particular spot. Additionally, polymeric nanoparticles are used to maintain and regulate the release of the drug. The kind of polymer that was employed to create the polymer-based nanoparticles is the subject of the current review study for their classification, characteristics, and applications of nanoparticles (NPs), which come in a variety of forms and sizes. Nanoparticles, which have diameters in the nm range, are the simplest type of structure. An NPs is well-defined as a collective group of molecules compelled composed of a structural range of fewer than 100nm. As of their higher solubility, smaller size, and improved penetrability, NPs are commonly used for a variety of dosage formulations. Some of the processes used to generate NPs include the Solvent Evaporation Method, Double Emulsion method, Salting Out Method, Precipitation Method, ionic gelation Method and Polymerization Method. The aim and objective of this review article is to give a concise information about polymeric nanoparticles including method of preparation and their applications.

Keywords: *Polymeric Nanoparticles, Nanotechnology, Polymerization, Drug delivery and FTIR*

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1. INTRODUCTION

In many disease conditions, the delivery of therapeutic compounds to the correct site is a major hurdle. Delivery of therapeutic compounds to the right place is a serious difficulty in many diseases. The use of traditional medicine is characterized by variable biodistribution, limited efficacy, unwanted side effects, and lack of choosiness. In addition, the drug delivery system (DDS) provides protection from degradation or quick clearance. It also increases the concentration of the drug in the target tissue. So, lesser amounts of the drug are needed. This type of treatment is necessary when there is a difference between the quantity and concentration of the drug and the outcome or toxic effect of the treatment. Targeting specific cells or tissues using specific drug-attached scaffolds is an extra robust method in drug delivery systems. Such an approach is called as cell and tissue-specific targeting. Reducing the size of the target formulation or designing the pathway for appropriate drug delivery systems is an additional essential & successful method that systems the basis of nanotechnology. The science of Drug delivery is an ever-evolving field with research going on in transdermal delivery and nanotechnology.[1,2]The beginning "nano" has been increasingly useful to many areas of information during the earlier period. Nano-science, nanotech, biomaterials, and nano-chemistry remain just a several of the novel related phrases which become common concept in scientific studies, popular literature, and newspapers, while becoming familiar to a broad audience, including non-experts. The preface is derived from the early Greek word, which comes from Latin "nanus", which means dwarf and, by implication, very little. It's being used to signify a conversion feature of 109 times as in the "International System of Units" (SI) convention. As a result, the nanosized universe is normally assessed using nanometers (1nm = 10^{-9} m) which includes systems that are larger than molecular dimensions but smaller than macroscopic dimensions (normally > 1 nanometer and 100 nanometers). Nano-technology is the knowledge of very small; nanotechnology is the science of the extremely short. It includes the consumption and use of ingredients arranged on a very minor scale. At this size, particles and molecules perform differently, allowing for several unpredicted and fascinating submissions. It consents to the making of novel constituents, notably for therapeutic usages, when traditional procedures might be limited. Nanotechnologies must never be observed as a distinct tactic with partial submission. Nanotechnology does not just mean exceedingly small systems and goods, despite its moniker as the "little science." Bulk materials and broad surfaces frequently integrate nanoscale characteristics. Nanotechnology is the study, progress, and implementation of material somewhere at nuclear, molecular, and organic compound levels to generate novel nanoscale ingredients.[3] Pharmaceuticals nanoparticles have hard, submicron-size drug carriers (less than 100 nm in diameter) which can be recyclable or not. NPs is a term that encompasses both nano-spheres and nano-capsules. Nano-spheres are indeed a medium classification in which the medicine is evenly spread, whereas nano-capsules are a method in which the medication is encased in a distinct polymer membrane. The classification, technique of manufacture, characterization, applications, health implications, and pharmacologic features of nanoparticles are all covered in this review. [4,5]

2. POLYMER BASED NANOPARTICLES

The solid colloidal particles in size from 1nm to 1000nm are called polymeric nanoparticles. In this type of technology, the drug is dissolved, enclosed or attached into matrix of nanoparticles. The surface of these structures is very large. Polymer is very useful in pharmaceutical for preparing the macro and small size molecules.[6] Polymeric nanoparticles consist of natural polymer (e.g., gelatine, chitosan etc.) which are biodegradable and biocompliment, or synthetic polymers (e.g., poly lactides, poly acryl cyano acrylates etc.). The choice of material for polymeric nanoparticles is determined by the factors below.

- Particle Size and surface features required
- Drug and other active ingredients solubility and stability
- Biodegradability standard
- Biocompatibility and toxicity
- Required profile of drug release[6]

2.1 Types of polymer-based nanoparticles

Polymer based nanoparticles are given for much polymeric form, but mainly it can be classified into two types:

- **Nanospheres**
- **Nanocapsules**

2.1.1 Nanocapsules

They act as drug reservoir, due to their vesicular structure, in which the retained active pharmaceutical materials are reserved in an aqueous and non-aqueous liquid centrally located in the vesicle cavity, then surrounded by the hardened polymeric shell.

2.1.2 Nanospheres

They can be defined as a solid/mass of matrix polymers. In additional words, any nanosphere may represented as a total polymeric circular mass in which, as effect, 7 drug particles may be surrounded within the domain centre or adsorbed at the mass surface.[7]

2.2 Structure of Polymeric NPs (Nanoparticle)

Polymeric NPs can be defined as colloidal structures, typically ranging in size from about 5-10 nanometer to a greater size limit of 1000 nanometers, although the general range is 100-500 nanometers. The term "polymer nanoparticles" is a general term, which is used for all types of nanoparticles. Polymer nanospheres are particles in a matrix, i.e., particles that are dense in mass. In addition, they can serve as carriers of other biologically active molecules, which can be absorbed on the surface of the beads or encapsulated into particles. Here, the biologically active ingredients include drugs, genes, nucleic acids, fluorescents and other functional ingredients. Polymer nanocapsules are vesicular systems, that contain the bioactive agent in an aqueous core and are encased in a polymer shell, as opposed to polymer nanospheres. A diagram illustrating the polymer nanoparticles is shown in Figure. 1.[6]

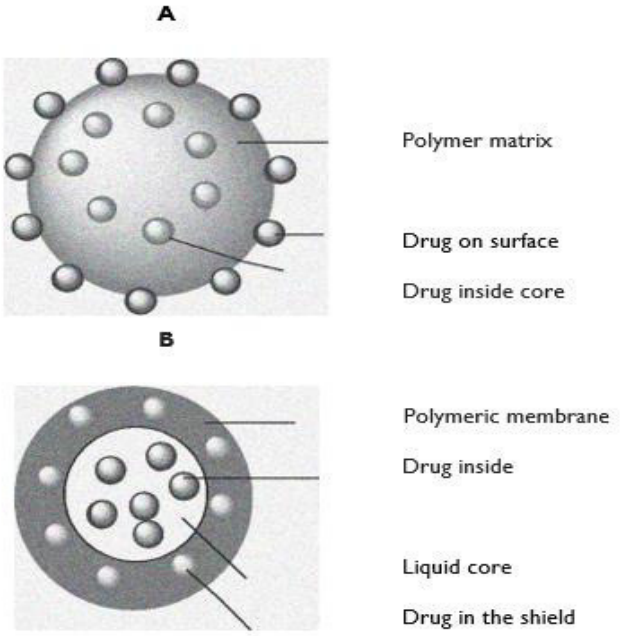

Fig 1. Polymer nanoparticle structures. (A) Polymer nanoparticles (B) Polymer nanocapsules. [6]

3. CLASSIFICATION OF POLYMERIC NANOPARTICLE

Nanoparticles are roughly divided into three classifications[7]

• ***1-Dimensional***

1-dimensional systems (thin film or surface fabrication) have been in usage for several years. Thin films (size 1-100 nanometers) or single layers are now commonplace in the area of solar cell offerings, and various technology applications like as biological and chemical sensors, data storage systems, optical and magneto-optical devices, and optical systems.

• ***2-Dimensional***

2-dimensional (2D) NPs have 2 dimensions outside of the nanometric size range. These particles have thin-film, nanosheet, or nanocoating properties. They are widely used in nanostructured devices such as sensors and nanoreactors.[8] Carbon nanotubes (CNT) are well-known examples of such nanoparticles with two-dimensional structure. They are made of a 2D layer of graphite that has been rolled to form a tubular structure.

• ***3-Dimensional***

3-dimensional (3D) NPs display nanoscale feature internally even though none of the three external dimensions are at nanoscale. This category includes fibrous, multilayer, and polycrystalline materials as well as some powders. Lower-dimensional nanoparticle elements serve as the structural building blocks of these objects. 3D nanoparticles are extremely significant and have numerous uses in contemporary nanotechnology. Dendrimers and fullerenes, also referred to as carbon 60, are two such promising particles. [8]

3.1 Organic nanoparticles

Dendrimers, liposomes, micelles and ferritin, etc. are commonly known as the organic nanoparticles or polymers. These NPs are non-toxic, biodegradable, and some particles, like micelles and liposomes, have hollow centres that are referred to as nanocapsules. These particles are also sensitive to electromagnetic radiation, including heat and light (Figure 2).[9] They are an efficient carrier for drug transport because of their particular properties. In addition to the usual properties like size, content, surface shape, and delivery systems, their drug volume, consistency, and entrapped medication or adsorbed drug system, regulate their variety of submissions and effectiveness. Organic nanoparticles are commonly employed in medical applications like the DDS, since they are effective and can be administered to different body parts, a process called targeted drug administration. Organic NPs of Rhodiarome, cholesterol, and Rhovanil have been produced in several micro-emulsions "(AOT/heptane/water; Triton / decanol / water ; CTABr / hexanol/water)" by a straight precipitate to the main ingredient in an aqueous essential underneath ongoing ultrasonication. [10]

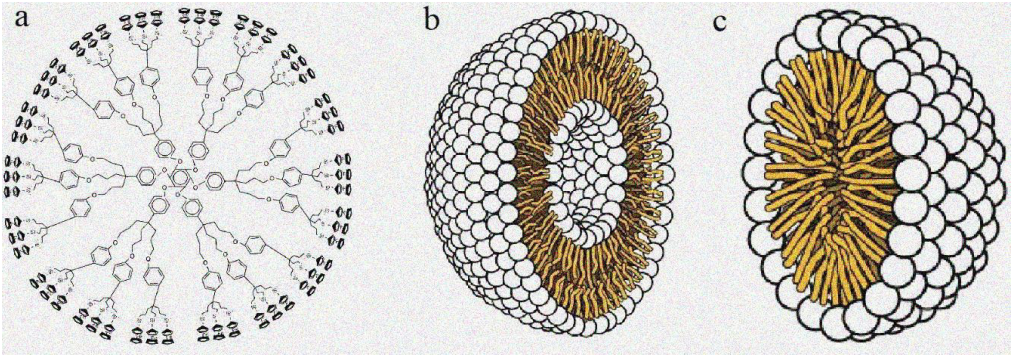

Fig 2. A. Dendrimer, B. Liposome, C. micelles. [9]

3.2 Inorganic NPs

Inorganic NPs are non-carbon nanoparticles. Metal oxide-based NPs make up inorganic NPs.

1. Metal-based: - NPs created from metal utilizing destruction or reconstructive procedures to reach nanometric sizes are called metal-based nanoparticles. NPs can be created out of almost any metal. [11] NPs have features with a size range from 10 to 100nm, a high specific Surface area (SA): amorphous structures, surface charge, pore size, density, spherical and cylindrical color, crystalline, size ratio, sensitivity, and reactivity, to ecological factor such as humidity, thermal, air and natural light, and more.

2. Metal-based Oxide: Metal-oxide NPs have been developed to modify the property of metal-based NPs. Within the existence of oxygen at room temperature, iron nanoparticles, for example, immediately oxidize to iron oxide (Fe_2O_3), boosting their reaction. Due to their improved effectiveness and reactivity, metal-oxide NPs have been widely used. [12] The most commonly manufactured oxides are ZnO (zinc oxide), CeO_2 (cerium oxide), SiO_2 (silicon dioxide), Fe3O4 (magnetite), $Fe2O_3$ (iron oxide), TiO_2 (titanium oxide), and Al_2O_3 (aluminium oxide). These NPs have superior assets when related to their metal parts .[13]

3. Carbon-based: NPs made totally of carbon is called C-based NPs. [14] As illustrated in Figure 2, carbon nanotubes (CNT), Fullerenes carbon black , graphene, carbon nanofibers, occasionally started carbon on the nanoscale are split into Fullerenes, carbon nanofiber, graphene, CNT (carbon nanotubes), carbon black, too occasionally started C nano-size.

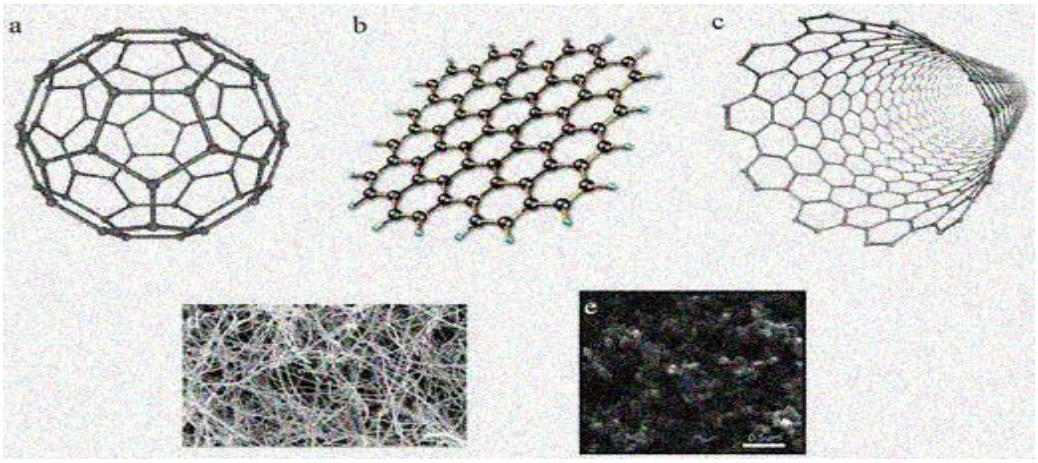

Fig 3. graphene, fullerenes, carbon nanotubes, carbon nanofibers, and carbon black [14]

1. Graphene. This is a 2-dimensional hexagonal honeycomb lattice-complete composed of C-atoms in a plain hexagonal network. A graphene sheet normally has a thickness of about 1 nanometer.

2. Carbon-nanotubes (CNTs) are extremely small carbon tubes. Looping a graphite nano-foil with a honeycomb lattice of C-molecules in hollowed cylinders which produces carbon nanotubes and had small as 0.7 nanometers for single-layer CNT & 100 nanometers for multi-layer CNTs too ranges changing to certain mm to many cm. They might be empty or locked with half C_{60} molecules.

3. Carbon nanofibers are produced from the same graphene nano foil as carbon nanotubes, but instead of cylindrical tubes, they are coiled into a cone or cup shape.

4. PREPARATION OF POLYMERIC NANOPARTICLES

The drug to be delivered and the polymer's physicochemical qualities define the best manufacturing technique for nanoparticles. Nanoparticles can be made in several ways:

4.1 Solvent Evaporation Method

In this process polymer is mixed in an organic solvent: - chloroform, dichloromethane and ethyl acetate, and it can also be used to disperse the hydrophobic medication in this operation. An o/w mixture is created by combining the drug or polymer solution including a surface-active agent or mixing materials. The natural solute is removed by decreasing the

burden or through constant stirring just after the development of something like a stable emulsion. The kind and composition of the stabilizing agent, the speed of the mixer, and the polymer type all had an impact on particle size. [15] Increased homogenization or ultrasonication are commonly used to obtain tiny particle size. [16] In one study, polymer-drug nanoparticles were organized using an emulsion solvent evaporation technique. The polymer-drug NPs included Eudragit E 100 and ketoprofen. It is necessary to construct extra stable particles by using an aggregate of protecting excipient lactose and glucose as the distributed organic solvent.[17] Atorvastatin or Candesartan cilexetil, both from category II of the classification of biopharmaceuticals system, are formed by evaporating the solvent in Tween 80 medium, atomic number 11, sodium carboxymethylcellulose, dodecyl sulfate, macrogol 6000, and sodium carboxymethyl dextran, forty samples of atorvastatin atomic number 20 (I) and candesartan cilexetil (II). A nanoresins spectrometer was used to analyze all of the samples. Cilexetil, Candesartan, and atorvastatin nanoparticles prepared in this way are claimed to have increased bioavailability when used in nanoparticle formulations.[18]

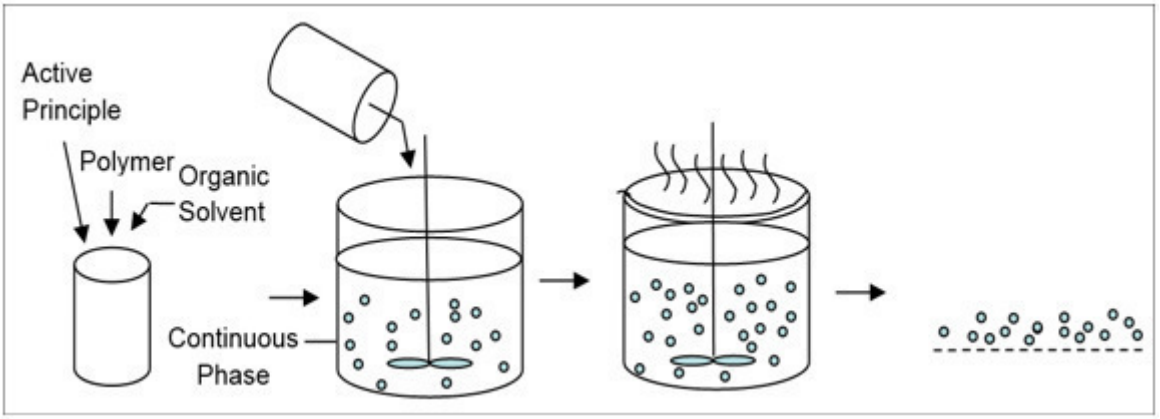

Fig 4. Illustrate the solvent evaporation method in brief in this fig. firstly prepare organic and aqueous phase after that mix the organic and aqueous phase and then string done and polymeric nanoparticles are formed. [18]

4.2 Spontaneous Emulsification Method

This process was established from the solvent evaporation process, which uses a solvent soluble in water along with a few amounts of organic solvent (non-miscible with water) as well as the oil phase. Interstitial vibration is created during the rapid diffusion of the solvent between both two stages, which can finally lead to the development of tiny particles. The increasing amount of solvent combined with water results in a smaller particle size. This technique can be used for drugs that are hydrophobic or hydrophilic. Some w/o/w emulsions must be designed by the drug mixed in the inner aqueous phase in the case of hydrophilic drugs.[19]

4.3 Double Emulsion Method

The hydrophobic and water-soluble drugs are encapsulated in PLGA-based particles via a double or single emulsion. In short, the drug is mixed or emulsified with the polymer in the organic stage before being mixed in the aqueous stage. After the solvent had evaporated, the beads were washed and centrifuged to collect them for long-term storage and lyophilization[20]. To enhance the encapsulation efficacy of DNR NPs in PLGA and PDLLA, a series of daunorubicin-loaded NPs using a modified diffusion method that included a partly hydrophilic organic solvent in the granule formation. These findings could be useful in a variety of situations. The preparation of hydrophilic chemotherapeutic drug nanoparticles necessitates effective conveyance to tumor cells to a continual release at a specific site.[21]

Advantages

It offers the benefit of encapsulation of both hydrophobic and hydrophilic activities.

Disadvantages

A. Large particles
B. Two-step procedure.
C. Leak of the water-soluble in the exterior aqueous phase.
D. Tough to measure up[22]

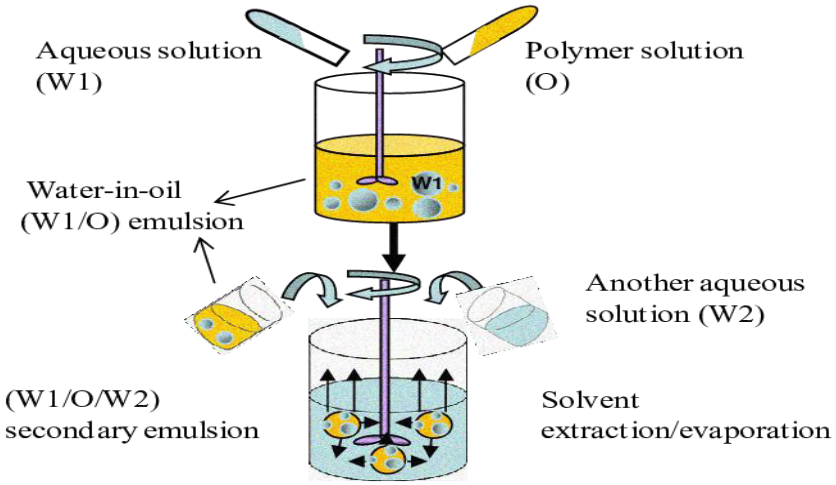

Fig 5. Illustrate the Double-emulsion method in this fig. show prepare double emulsion and after that both emulsion is mix properly and evaporate solvent and stiring done and collect polymeric nanoparticles [21]

4.4 Salting Out Method

By salting out a water-miscible solvent in the aqueous solution, NP can be separated. [23] The salting-out method (electrolytes and nonelectrolyte sucrose or calcium chloride, or magnesium chloride) and colloidal stabilizer PVP (polyvinylpyrrolidone) and hydroxyethyl cellulose are dissolved in a solvent, then mixed into an aqueous gel having the polymer or drug. This O/W mixture is diluted with the aquatic or aqueous stage to improve solvent dispersion, resulting in the development of nanospheres. Electrolyte concentration, polymer content in the organic stage, stabilizer form, stirring rate, and the external/internal stage ratio are all variables that can be modified. [24] This technique creates high-efficiency Ethylcellulose, PLA, and Poly(methacrylic) acid nanospheres and is easy to scale up. This approach may help heat-sensitive materials and it does not necessitate a rise in temperature. The method's limitations include its inability to clean lipophilic drugs and the time it takes to clean nanoparticles. [25] The salt immersion (SO) technique was used to load paracetamol into the Eudragit S100. The polymer was Eudragit S100 (ED). PCM and polymers were mixed in ethanol at different polymer-to-drug ratios of the three preparations, 1:3 was deemed the best, is an 80.3 % drug content and a 99.8 % yield. The loading capacity of the 1:3 formulations is said to be greater. $ZnSO_4$ is used as a stabilizer. As a release agent, $7H_2O$ is used, and ethanol is used as a solvent.[26] Ibuprofen-loaded NPs formed by three industrial processes- emulsification-diffusion, nanoprecipitation, and salting were tested at the experimental scale by increasing the volume of the research laboratory. As polymers and emulsifiers, poly (vinyl alcohol) & Eudragit® L100 was used.[27]

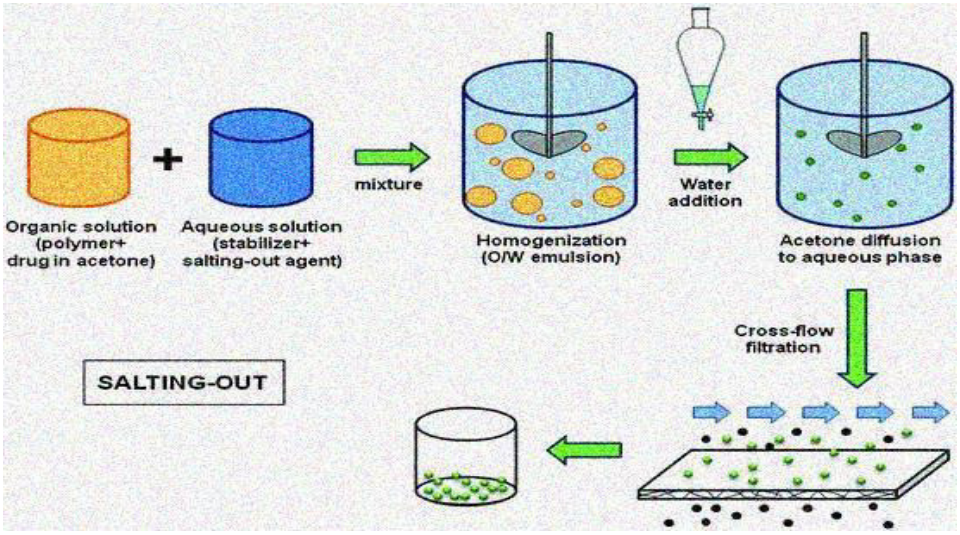

Fig 6. Illustrate Salting-Out Method in this method two solution are prepared organic solution (Polymer + Drug+ solvent) and Aqueous solution (stabilizer + salting out agent) after that both solution is mix together and homogenization done and add water for diffusion of Acetone(solvent) and filter the solution and collect polymeric nanoparticles [27]

4.5 Emulsion-Diffusion Method

This is yet another popular method for producing NPs. The encapsulated polymer is mixed in a partly water-soluble solvent (like benzyl alcohol) or saturated by water to check the early heat transfer equilibrium of the two liquids. The solvent phase containing water of the polymer is then mixed in water containing the stabilizer, which leads to the diffusion of the solvent to the outer stage and the development of nanocapsules or nanospheres, depending on the oil to polymer ratio. In conclusion, depending on the boiling point, evaporation or filtration are used to remove the solvent. This

technology has many advantages, including B. high efficiency of encapsulation (typically 70%), There is no need to homogenise, greater reproducibility from batch to batch, simple scaling, a limited size distribution.

4.6 Solvent Displacement Technique

It is demonstrated by the deposition of a preformed polymer from such an organic solvent and the dispersion of a solvent in water-soluble material in the occurrence or absence of surface-active agents. In acetone or ethanol, a water-miscible semi-polar solvent, polymers, pharmaceuticals, and lipophilic surfactants are dissolved. The solution is transferred or inserted into an aqueous medium in a magnetically stirred stabilizer. NPs are shaped as a result of the quick solvent diffusion process. The solvent is subsequently extracted after the suspension at decreased pressure. The amount at which the organic phase is presented in the aqueous phase influences particle size. According to a study, increasing the mixing rate reduces particle size and drug entrapment and decreases particle size or drug entrapment. [28] The nanoprecipitation approach is ideally suited to the majority of poorly dissolving medicines. Nano-sphere size and drug release can be effectively altered by regulating preparation limitations. The production of smaller nanospheres improves dramatically as the polymer concentration is increased. [29] Starch NPs were created using local maize starch. After being modified, the mixture is carried out using a Solvent displacement. The modification involved using an alkaline aqueous phase as the ethanol and solvent as the natural non-solvent. It approaches a good way to ensure simpler or more reproducible Starch NPs education without consuming additional solvents.[30]

4.7 Ionic gelation method

The utilization of biodegradable water-soluble polymers including sodium alginate, chitosan, and gelatin in the creation of nanoparticles has been investigated in several research. The utilization of biodegradable water-soluble polymers including, sodium alginate, chitosan, and gelatin in the creation of nanoparticles has been investigated in several research.[31,32] Two aqueous phases are used in the technique, one of which contains the polymer chitosan and the other of which contains polyanionic. To create nanometer-sized coacervates, a positively charged chitosan amino group is combined with a negatively charged tripolyphosphate. Coacervates form when two aqueous phases are electrostatically connected, whereas ionic interaction circumstances at room temperature promote ionic gelation, which results in a liquid-to-gel transition. Coacervation was used to create gelatine/submicron nanoparticles (GN/SP) as drug carriers. A 0.5 % aqueous solution (w/v) of gelatine was used in a study, along with a solvent-free binary structure of ethanol and acetone. The synthesis of nanoparticles is optimized for the solvent-free system type and pH 7 produced the least particle size of 55.67 nanometers in an anhydrous medium and a swollen particle size of 776 nanometers (38.57) in an aqueous phase, by a zeta potential in the water. The swelling percentage of 13.95 confirmed the particles' cross-linked hydrogel nature. [33] Modified ionotropic coacervation or gelation was used to generate microscopic nano-reservoir systems containing gatifloxacin. It was optimized using the experimental design using the Box Behnken 3-level, 3-factor statistical design. The self-determining variables calculated the quantity of bioadhesive. Polymers- ALG, CS, the quantity of drug in a preparation. [34,35]

4.8 Example of various polymer used for formulation of polymeric nanoparticles

Table No.1 Explained the various polymers are used for preparation of polymeric nanoparticles for various type of disease

"S.N	Formulation	Polymers	Use	Reference
1.	Microencapsulation of acyclovir into Eudragit S100 using emulsion- solvent evaporation method	Eudragit s100	Anti-viral drug	49
2.	Formulation of PLGA Polymeric Nanosuspension containing Pramipexole Dihydrochloride for improved treatment of Parkinson's Diseases	PLGA	Parkinson's Diseases	50
3.	Formulation and evaluation of irbesartan nanosuspension for dissolution enhancement	Irbesartan	Angiotensin receptor blocker	51
4	Formulation and Physical Evaluation of Castor Oil based Nanoemulsion for Diclofenac Sodium Delivery System	Castor oil	Nonsteroidal anti-inflammatory Drugs	52
5.	Fabrication and Character Study of the Anticancer Drug Paclitaxel (Taxol): PLGA nanoparticles - The benefaction for the modern therapeutic area	PLGA	Anticancer	53
6.	Solid Dispersion Characteristics of Whiteleg Shrimp (Litopenaeus vannamei) Extracted Chitosan with HPMC and PVP K-30 as Anti-cholesterol Agents	HPMC AND PVP-30	Anti-cholesterol	54
7.	Formulation and Evaluation of Mucoadhesive Buccal Tablets of Curcumin and its Bioavailability Study	Guar gum, Xanthan gum, HPMC E15	Mucoadhesive Buccal tablet	55
8.	Physicochemical Characterization of Bi-Layered Terbutaline Sulfate Tablets for Chronotherapeutic Pulsatile Drug Delivery Design Based on Natural and Synthetic Polymer using Direct Compression Technique	HPMC K100M, ethyl cellulose, karaya gum.	Pulmonary disease	56
9.	Design and characterization of valsartan Co-crystals to improve its aqueous solubility and dissolution behaviour	succinic acid	Improve bioavailability for heart diseases	57
10.	Formulation and development of cephalexin oral reconstitutable suspension	xanthan gum, HPMC	Beta lactam antibiotic"	58

4.9 Polymerization of monomers

In this method, during the polymerization of monomers in an aqueous solution, the medication is absorbed also by absorption in the NPs or by mixing in a polymerization medium. The NPs suspension is purified or re-suspended in an isotonic surface-active agent-free medium after different stabilizers and surfactants required for polymerization are removed using ultracentrifugation. This method for making poly (alkyl cyanoacrylate) or poly-butyl cyanoacrylate NPs was early reported. [36] The shape or size of capsules is pretentious by the number of surfactants used. [37]

5. CHARACTERIZATION OF POLYMERIC NANOPARTICLES

5.1 Ultraviolet absorption spectroscopy

Absorption spectroscopy is used to identify a solution's optical property. Whenever lights are flashed across the stock solution, the change in absorbance is recorded. The absorption at each wavelength is recorded as the wavelengths are altered.[20] In a study, after UV-visible spectroscopy revealed a favorable surface, plasmon with high band intensity or peak in the range of 216-265 nm is used. [38] The silver NPs were produced and chemically characterised using UV vis spectroscopy, the obtained silver NPs ranged in size from 2.3 nm to 3.7 nm.[39]

5.2 FTIR spectroscopy

FTIR spectrometry is used for the chemical functional group analysis on the surface of nanoparticles. IR radiation is sent onto the sample in the FTIR spectroscopy. While some of this energy is absorbed by the sample, some of it also passes, and thus, absorption and transmission spectra of the molecules come out. These absorption/transmission spectra are the characteristic spectra of the molecules in the sample and define the absorption/transmission peaks of the material. These peaks agree to the vibrational frequencies of the bonds among the atoms in the material. The intensity of the peaks gives information about the amount of the material as well as the wavelength in which the peaks appear in the spectrum defining the bonds between the atoms. For this reason, FTIR is a useful method to characterize the material[40]

5.3 Particle Size

The properties of NPs are mainly assessed based on the particle size distribution and morphology. The NPs' size and morphological characteristics can be identified using electron microscopy. Various tools can easily identify the use of NPs in drug delivery and drug targeting. It has previously been described that the particle size of NPs has a significant influence on drug release.

Table 2 Various nanoparticle characterization tools and methods[41]

"Parameter	Characterization method
Carrier-drug interaction	Differential scanning calorimetry
Charge determination	Laser Doppler Anemometry Zeta potentiometer
Chemical analysis of surface	Static secondary ion mass spectrometry sorptometer
Drug Stability	Bioassay of drug extracted from Nanoparticles Chemical analysis of drug
Nanoparticle dispersion stability	Critical flocculation temperature (CFT) Atomic force microscopy
Particle size and distribution	Laser diffractometry Photon correlation spectroscopy (PCS) Scanning electron microscopy Transmission electron microscopy
Release profile	In vitro release characteristics under physiologic and sink conditions
Surface hydrophobicity	Rose Bengal (dye) binding Water contact angle measurement X-ray photoelectron spectroscopy"

Table 2 Illustrate the characterization of polymeric nanoparticles such as carrier drug interaction are evaluate by DSC; Charge is determined by Laser Doppler Anemometry and a Zeta potentiometer; a static secondary ion mass spectrometry sorptometer analyses the chemical's surface; Drug stability by drug chemical analysis and drug bioassay of drug extracted from nanoparticles; Atomic force microscopy, Critical flocculation temperature (CFT), and nanoparticle dispersion stability; Particle size and distribution using scanning electron microscopy, laser diffractometry, PCS, and transmission electron microscopy; Release profile by In vitro release characteristics under physiologic and sink conditions; Surface hydrophobicity by Rose Bengal (dye) binding, Water contact angle measurement, X-ray photoelectron spectroscopy. Smaller NPs with a greater surface area result in quicker release of the drug. The loaded drug causes significant drug release when the revealed surface of the particle. In contrast, there is a slower diffusion of larger particles in the nanoparticle drug. As a result, when the nanoparticle dispersion is stored and transported, the tiny particles have a tendency to aggregate. Therefore, it is necessary to find a compromise with both small nanoparticle size and maximum stability.[42] Additionally, size of the particles can have an impact on depolymerization. For instance, researchers found that within Vitro, poly (lactic-co-glycolic acid) decomposition enhanced as the size of the particles increased.[43] The development of analytical technology has created it possible to determine the size of NPs using a various method, as will be covered below.

5.4 Dynamic Light Scattering (DLS)

The quickest and most widely used method for particle size is needed for current research. Brown nanoparticle sizes in nano and sub-micron colloidal suspensions are frequently determined using the quickest and most popular techniques,

such as "(PCS) photon correlation spectroscopy" or "(DLS) dynamic light scattering". When subjected to light source, this technical solution of sphere-shaped particles moving in a doppler shift is caused by Brownian motion(laser). When trying to move particles exposed to light sources in this way, the incident light's wavelength is altered. The rate of change of the wavelength determines the particle size. The particle sizes and movement of the particles in the medium are estimated with the aid of these parameters, which can also be used to measure the diffusion coefficient of particles and calculate the correlation function. "Dynamic light scattering (DLS)" provides the most commonly used technique to accurately estimate size of the particles and their distribution.[44]

5.5 Scanning electron microscope

SEM photographs of ARTM (artemether) alone presented characteristic crystalline blocks of artemether, although in SDs of artemether, scanning electron microscope presented crystalline structures of artemether were reduced in size having no sharp ends in both freeze-dried mixtures and physical. SEM presented the development of flakes on behalf of amorphous cumulations by smooth surfaces, while the situation freeze-dried combination presented a glassy appearance adding size reduction or embedment. Scanning electron microscope in Cremophor-A25 relieved by Poloxamer 188, presented flakes taking no smooth superficial, while its freeze-dried combination showed improved uneven shaped glassy presence, similar to the result of artemether as found earlier[45]. The surface morphology of ARTM, lumefantrine and the preparation was considered using SEM by sprinkling S-SNEDDS powder on a dual adhesive plate fixed in an aluminum stub, more coated by platinum 10o A thick below high vacuum. zinc oxide NPs were set with and without surface-active agents. The surfactant was PVA, and the Nanopowder was analyzed using Scanning Electron Microscopy. According to the characterization results, the traditional technique of preparation, without any surfactant, is strongly influenced by particle agglomeration and particle separation is inadequate. However, when a surfactant is used, particle agglomeration is reduced and particle separation is improved.[46]**.** SEM microscopy was used to prepare and characterize copper nanoparticles (SEM). The paper shows how to make copper nanoparticles by reducing copper salts in an aqueous media in a simple, easy, and important way. Only when PVA is used does the absorption phenomenon in copper NPs owing to SPR ("surface plasmon resonance") become noticeable at about 580–600 nm.[47]

5.6 Transmission electron microscopy (TEM)

Microscopy in which an ultra-thin object interacts with a stream of electrons is known as transmission electron microscopy (TEM). An image is greatly amplified or focussed towards a visualized device for detection, for example, a fluorescence screen, a photographic film layer, or a sensor, such as a camera, by interacting with the electrons traveling through the sample. Iron nanoparticles made by various methods of iron carbonyl breakdown are compared. By combining the particle size measurements obtained by Transmission electron microscopy, the specific magnetization of particles generated in different ways was discovered. For heterogeneously nucleated particles, the results reveal high values of specific magnetization[48]. TEM research was used to explore the mechanism of antibacterial action of curcumin nanoparticles, which demonstrated that these particles entered the bacterial cell by fully shattering the cell wall, resulting in cell death.

5.7 Atomic Force Microscopy

This method is called "atomic force microscopy", a type of ultra-high resolution scanning probe microscope, with resolutions described on the instruction of nanometer fractions, greater than 100 times the optical diffraction limit. It involves creating an image of the surface using a probe that detects the sample. AFM has a very high resolution in particle diameter. measurement techniques and is based on the physiological monitoring of a sample at the submicron scale with an atomic scale probe tip.[49] Based on the properties, samples are usually searched in contact or non-contact methods. In interaction mode, the probe touches the sample to create a detailed map; in a non-contact method, it begins to move over the conducting material. One of AFM's key benefits is its capacity to image non-conductive. samples without special processing. This feature enables fine imagination of biological & polymeric micro and nanostructures.[50] Additionally, atomic force microscopy provides the most precise size description, size distribution, and real image that aids in understanding the effects of different biological conditions (without the use of mathematical calculations). [51]

5.8 Surface Charge

The interaction of NPs with the biological atmosphere and their electrostatic forces by bioactive substances are determined by the surface charge and intensity. The zeta potential is typically used to analyze the constancy of colloidal materials. Surface charge can be estimated indirectly using zeta potential. This can be discovered by assessing the possible discrepancy between the shear plane as well as the outer Helmholtz field. Therefore, the zeta potential of colloid-based dispersions aids in directly assessing their storage stability. To ensure stability and prevent particle aggregation, a high zeta potential value is attained. The surface hydrophobicity and characteristics of the material coated on the surface or contained in nanocapsules can be evaluated using the zeta potential value.[52]

5.9 Surface Hydrophobicity

It can be identified by methods such as chromatography with hydrophobic interactions, two-phase separation, probe adsorption, contact angle measurement, and so on. Recent research advances have resulted in the growth of a number of highly analytical tools for analysing the surface properties of nanoparticles. Advanced technologies, such as x-ray, (PCS) Photon correlation spectrometry, can not only identify the hydrophobicity of a surface but also identify specific chemical components on the surface of NPs. [53]

5.10 Drug Release

It is critical to identify the rate of drug administration, & most delivery methods require that the drug and delivery vehicle be kept apart. The drug concentration bound for every mass of polymer is defined as the drug loading capacity of NPs. To determine these parameters, different systems such as UV spectroscopy or HPLC Ultrafiltration, gel filtration, or centrifugal ultrafiltration are used after ultracentrifugation.[54] Drug release analysis methods are similar to drug loading

analysis methods. which are evaluated more frequently over time to assess the drug release mechanism. [55]

5.11 Zeta sizer

The charge or charge of the surface, the NPs, influences how it interacts with their target. A zeta potentiometer is a device that detects the surface charge dispersal stability in a sol[n]. [56] A Difference Movement Analyzer are used to regulate the charge of the NPs in the gaseous phase (DMA). The findings show that permanently charged methyl methacrylate copolymer nanoparticles can be made in a repeatable fashion. The copolymer NPs reported may be beneficial because their particle size in nanometre choice and their surface charge is pH-independent. [57] Encapsulation of catechin in bioadhesive chitosan NPs (CS NPs) was tested for mucoadhesive possible, which leads to increased catechin oral bioavailability. A modified approach was used to synthesize and analyze CS NPs, a potential carrier for sustained release of bioactive. Catechin-loaded CS NPs have a positive zeta potential and smaller extent, indicating that they can offer bio adhesion in the GIT.[58]

5.12 X-ray diffraction (XRD)

XRD study for all the samples was completed by using a device. The capacities or situations of XRD involved the aiming of CuKα , by a power of 40 kV or a current of 30 mA. A changed arrangement of diverging or getting receiving and anti-scattering slits. By using a stage width of around 0.04° 2ϑ among 5° and 50°, the XRD shapes were found. XRD patterns of artemether presented identical durable typical diffraction peaks on 17.64°,2ϑ of 9.88°, 18.04°, or 19.68°. It indicates that ARTM is purely a crystalline compound. X-ray diffraction design of PEG6000 presented typical diffraction peaks on 2ϑ of 19.6° or 23.76° [59]

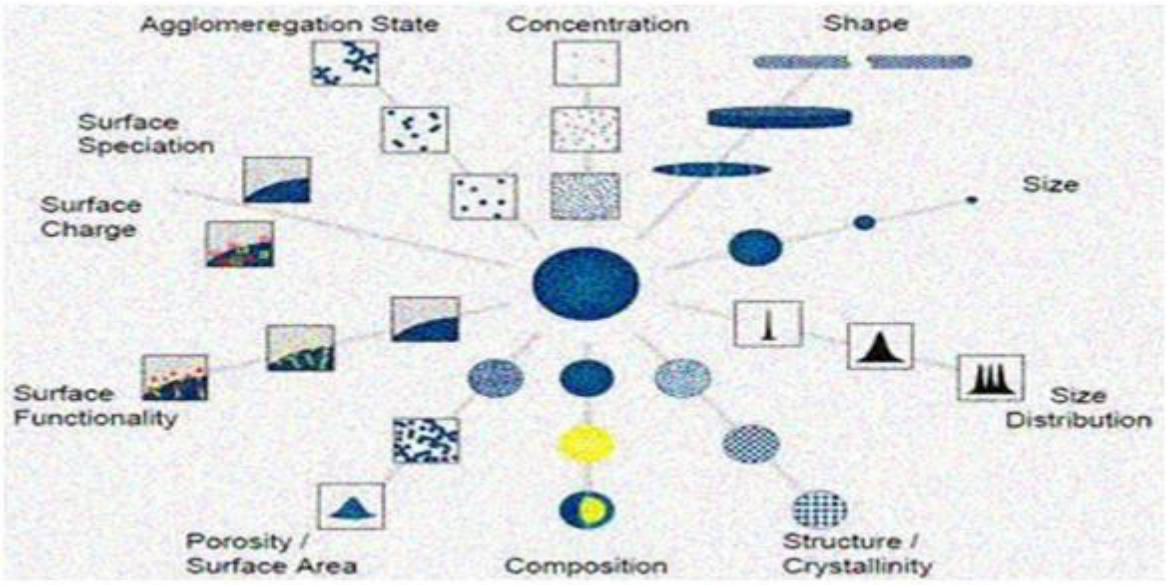

Fig 7 Characterization of Polymeric Nanoparticles[60]

Table 3. Many characterization methods for NPs in solid, liquid and gaseous phase [60]

"Characteristics	Solid	Liquid	Gaseous
Size	Electron microscope and laser diffraction for bulk samples	Photon correlation spectroscopy and centrifugation	SMPS and optical particle counter
Surface area	BET Isotherm	Simple titration and NMR experiments,	SMPS, DMA
Composition	XPS and chemical digestion followed by wet chemical analysis for bulk samples.	Chemical digestion for mass spectrometry, atomic emission spectroscopy and ion chromatography	Particles are collected for analysis by spectrometric or wet chemical techniques
Surface morphology	Image analysis of electron micrographs	Deposition onto a surface for electron microscopy	Capture particles electrostatically or by filtration for imaging using electron microscopy
Surface Charge	Zeta Potential	Zeta Potential	DMA
Crystallography	Powder X-ray or neutral diffraction	-	-
Concentration	-	-	CPC"

Table 3 illustrate the characterization method for solid, liquid, and gaseous phase nanoparticles Particle size of solid evaluate by Electron microscope and laser diffraction for bulk samples; determining the liquid's particle size using centrifugation and photon correlation spectroscopy; SMPS and an optical particle counter were used to measure gaseous particle size; BET isotherm, simple titration and NMR experiments, SMPS, and DMA were used to measure solid, liquid, and gaseous surface area; Composition of solid, liquid, gaseous by XPS and chemical digestion followed by wet chemical analysis for bulk

samples, Chemical digestion for mass spectrometry, atomic emission spectroscopy and ion chromatograph. Particles are collected for analysis by spectrometric or wet chemical techniques; Surface morphology of solid, liquid, gaseous by Image analysis of electron micrographs, deposition onto a surface for electron microscopy, Capture particles electrostatically or by filtration for imaging using electron microscopy; Surface charge of solid, liquid, gaseous by Zeta Potential Zeta Potential, DMA; Concentration of gaseous by CPC.

"BET – Brunauer–Emmett–Teller model, **CPC** – Condensation Particle Counter, **DMA** – Differential Mobility analyser, **NMR** – Nuclear Magnetic Resonance Spectroscopy, **SMPS** – Scanning Mobility Particle Sizer, **XPS** – X-ray Photoelectron Spectroscopy"

6. APPLICATION OF POLYMERIC NANOPARTICLES

NPS can be used in a range due to their exclusive features outlined earlier. Some of the most vital are recorded here.

6.1 Medicine

Nanotechnology, which makes use of nanoparticles, has stimulated the interest of scientists and researchers in the pharmaceutical and medical fields, as nanoparticles constitute the most basic kind of nano-bio materials. In medicinal applications, nanoparticles are utilized to treat cancer, [61] multicolor visual coding for biological assays, management of protein detection, cell, and biomolecule, surface disinfectant bio-pharmaceutical,[62,63] acticoat bandages, nanobarcodes for bioanalysis, etc. The following are some of the most mutual areas where nanoparticles are used in medicine: delivery of drugs, [64] therapy techniques,[65] diagnostic techniques,[66] anti-microbial systems, tumor cell targeting, cell repair, gene delivery,[67] diagnosis or bioimaging. [68] Polymeric nanoparticles are used to deliver medications [69,70] Because of the increased permeability and persistence, the nanocomposites have now been focused on tumors, inflammation regions, and antigen testing sites, allowing for both regulated drug release and disease-specific localization (EPR). [71] The NPs role in treatment techniques [72] mostly contains Combination treatment [73] for tumor action, the active drug delivery that enhanced pharmacokinetics [74] and decreased side effects, & some NPs-based chemotherapeutics developing with clinical and preclinical [75] progress. The antimicrobial capabilities of nanomaterials have been used to heal practically all Gram (+) and Gram (-), fungi, viruses, and bacteria. [76,77] Antimicrobic properties were examined by dissimilar metal NPs such as iron oxide,[78], silver, copper oxide, or, gold NPs. The rise of drug-resistant bacteria highlights the expansion of new antimicrobial medicines. As a result, many kinds of nanoparticles are quite good in their antibacterial properties. [79–82]

6.2 Energy, Electronics, Manufacturing, and Materials

Antibiotic resistance is increasing,[83,84] emphasizing the need for novel antimicrobial medicines. As a result, antibacterial properties have been demonstrated in a variety of metallic nanoparticles. [85] Nanostructures,[86] which hold a lot of promise in fuel cell manufacturing, nano colloidal catalysts, nanoclusters [87,88] in hydrogen storing, such as the electrocatalysts in polymer electrolyte fuel cells, and are all examples of nanoparticle applications in energy. [89] Nanoparticles are used in food, such as Nano tea [90] and Nanoceuticals Slim Shake Chocolate,[91] as well as bioprocessing, wearable electronics, and cosmetics. [92,93]

6.2 Energy Harvesting

The use of noble metal-based nanoparticles, particularly Au NPs and Ag NPs, demonstrates that research in this area is worthwhile. These structures have a broad variety of applications, with drug transport, features that improve the quality of radiation-based anticancer therapy, and molecular imaging, as well as molecules having bactericidal, fungicidal, and antiviral activities.

6.3 Mechanical industry

This can come in a variety range of mechanical strong structures. Titania, carbon-based NPs, and Alumina have all been successful in achieving the chosen mechanical features in coverings.

6.4 Food

NPs have been progressively incorporated in food packing to switch the ambient environment of food and keep it fresh or safe from microbial infection. Nowadays, inorganic and metal nanoparticles are widely used as replacements to fuel plastics in the food wrapper industry as they directly present antimicrobial materials on the covered film surface. [94]

6.5 Drug delivery

NPs involved in drug delivery – The NPs get the setup of treatments with better distribution to uptake the target cells and/or reduced toxicity of the free treatment to non-target tissues. [95]

6.6 Gene delivery

It is a method that plays an important part that can capably exist as a gene of attention in demand to prompt its fixed protein in appropriate host and host cell. Nowadays, there are different forms of main gene delivery that mostly employ viral paths like adenoviruses and retroviruses, nucleic acid transfection, and nucleic acid electroporation.[96]

6.7 Tumor treatment

There is a variation of NPs systems presently under inquiry to be useful in biomedical of the importance of cancer therapy. Some valuable metals (mostly silver and gold systems), and some Fe_3O_4 (magnetic oxides) acknowledged with much attention with quantum dots are called natural NPs. The exclusive process of UC nanoparticles may be used to start photosensitive healing mediators for submissions in tumor treatment.[97,98]

Advantages of Polymeric Nanoparticles

a) Improves the constancy of any volatile pharmaceutical agent, which can be easily and inexpensively manufactured in huge volumes using a variety of techniques.

b) In terms of effectiveness and efficiency, they represent a significant advancement over conventional oral & intravenous methods of administration.

c) Increases the concentration of pharmaceutical agents delivered to the desired area.
d) Polymeric nanoparticles are ideal applicants for tumor therapy, vaccine delivery, contraception, and clinical application delivery due to their polymer choice and ability to customize release of the drug.
e) Polymeric nanoparticles are easily incorporated into other drug delivery-related actions, like tissue - engineered.

7. CONCLUSION

For marketing purposes, nanoparticles are the most appealing. Antimicrobial, electrical, and biomedical products have all made use of them. In this paper, we present a comprehensive explanation of nanoparticle classification, as well as methodologies such as solvent evaporation, double-emulsion, dendrimers, and fullerenes. The nanoparticles' characterization is also discussed. In this study, a list of a few commonly utilized nanoparticles for medical, manufacturing, the environment, energy, and electronics has been discussed.

8. AUTHOR CONTRIBUTION STATEMENTS

Every author in the present manuscript has equally participated and contributed to the preparation of the manuscript. The author's contribution statement for the manuscript entitled "Review on Classification, Methods, and Characterization of Polymeric Nanoparticles with their Applications is as given below:

Mr. Dheerender Sharma: Mr. Sharma carried out the literature survey and designed the manuscript. Dr. Nishant Thakur: This idea was conceptualized by Nishant Thakur.Barsha Deb: Barsha Deb formatted and carried out a plagiarism check for the prepared manuscript.

9. CONFLICT OF INTEREST

Conflict of interest declared none.

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