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A BRIEF REVIEW ON VARIOUS ASPECTS OF NANOPARTICLES

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ABSTRACT: Nanotechnology is the idea of using medicines as a small machine inside the human body to detect and treat various diseases. Nanotechnology consists of deformation, separation, and consolidation of material from atoms and molecules due to its quick movement across the small capillaries. It allows immediate treatment to the targeted cells and also has fair use in oncology. Nanotechnology aims to reduce toxicity and side effects from healthy cells and increase the bioavailability and therapeutic effect in the targeted cells. But due to its ability to accumulate in body it can cause cell specific toxicity to overcome the challenge and create safe Nanoparticles green synthesis or preparation of Nanoparticles from biodegradable material like orange peel, eggshell etc are on trend. Nanoparticles based several vaccines also help us to combat global COVID-19 pandemic nanoparticle drug delivery are also becoming boon for some auto-immune diseases. This review describes the methods of preparation, characterization, classification, toxicity, and Nanoparticles applications.

INTRODUCTION: Pharmaceutical Nanoparticle is defined as solid, colloidal particle which is less than 1000 nm in diameter. Nanoparticles had its existence from Greek word Nano which signifies too little in size. In short term Nanoparticles are nanometric materials of size10-1000 nm (billionth part of meter) made up of different kinds of polymer. The term Nanoparticles are used in combination for nanospheres and Nano capsules where drug is dissolved, attached, encapsulated or entrapped to a matrix made up of nanoparticles [1].

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The important goals for designing of Nanoparticles are to manage particle size, surface properties and to deliver therapeutically active ingredients to have desired action of drug on active site at the optimum rate of dose regimen. The Nanoparticles and biomolecules like proteins, polynuclear acids have similar size which makes Nanoparticles a unique material with immense utility [2].

Pros of Nanoparticles:

- Increases bioavailability.
- Increases solubility of poorly soluble drugs.
- Allows direct treatment to the target cells.
- A small dose lowers the toxicity.
- Reduce exposure of drug in healthy tissue.
- Faster dissolution, greater absorption, and higher bioavailability.

Cons of Nanoparticles:

- During the biotransformation of polymeric carriers toxic metabolites are formed.
- Limited drug loading capacity in polymeric Nanoparticles.
- Difficulty of handling in case of liquid and dry formulations.

Application of Nanoparticles:

- Chemical and cosmetics
- Agriculture
- Nano medicines
- Electronics
- Conservation of energy
- Food packaging and preservation
- Sports
- Military
- Scientific tools
- Air and Water Remediation
- Diagnosis

Types of Nanoparticles Table 1:

Polymeric Nanoparticles:

Natural and synthetic materials are used in the synthesis of Polymeric materials which may be monomers or perforated polymers **Fig. 1**. They have wide variety of characteristic and structure. They have good biocompatibility and easy formulation parameters. Various technique used for polymeric Nanoparticles are emulsification, nanoprecipitation, ionic gelation and microfluidics [3, 4].

Polymeric Nanoparticles are termed as ideal co-delivery system because it has capability to carry both hydrophobic and hydrophilic therapeutic compound either by encapsulation, entrapment or chemical conjugation [5]. The different type of polymeric Nanoparticles is Polymer, Dendrimer, Polymer micelle and Nanosphere. The positives of this system allow them to deliver drugs, proteins and genetic material to the targeted tissues in the treatment of cancer, gene therapy and diagnostic. But the issue with particle aggregation and toxicity has been a problem for most polymeric NPs [6].

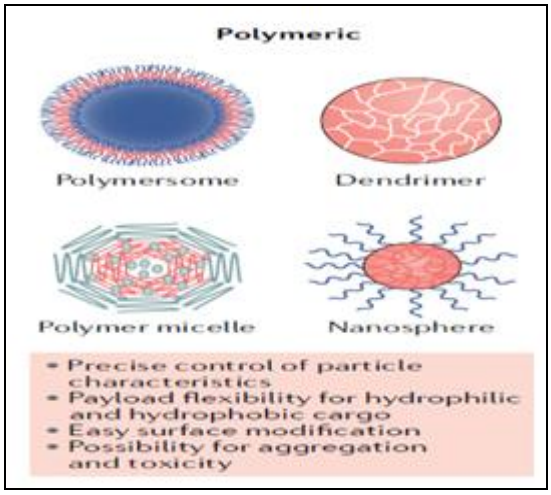

FIG. 1: POLYMERIC NANOPARTICLES

Inorganic Nanoparticles: The inorganic materials like iron, gold and silica are mostly used to produce nanostructure materials used for drug delivery and applications in imaging **Fig. 2**. Gold and iron Nanoparticles are most commonly and widely researched. The various forms used are nanospheres, nanorods, Nano stars, Nano shells and nanocages. They have different photo thermal and super magnetic properties at different shape and size which make them applicable in wide area [7, 8]. Other inorganic Nanoparticles are calcium phosphate and mesoporous silica which are used in drug and gene delivery [9]. The radioactive, magnetic, and plasmonic characteristics of inorganic NPs are useful in diagnostics, imaging and photo thermal therapies. They do have biocompatibility and stability, but low solubility and toxicity concerns of metals are limiting factors in clinical applications [10].

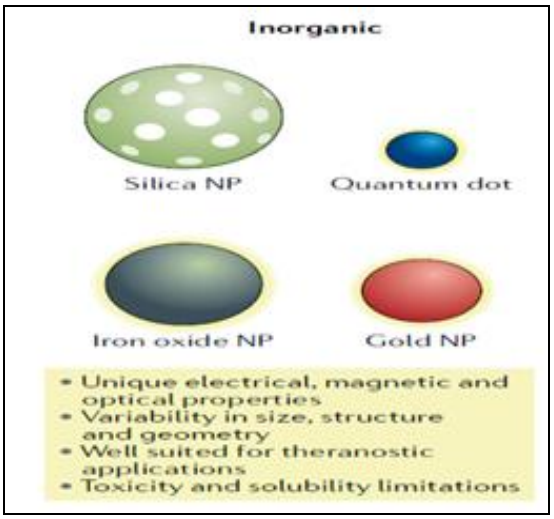

FIG 2: INORGANIC NANOPARTICLES

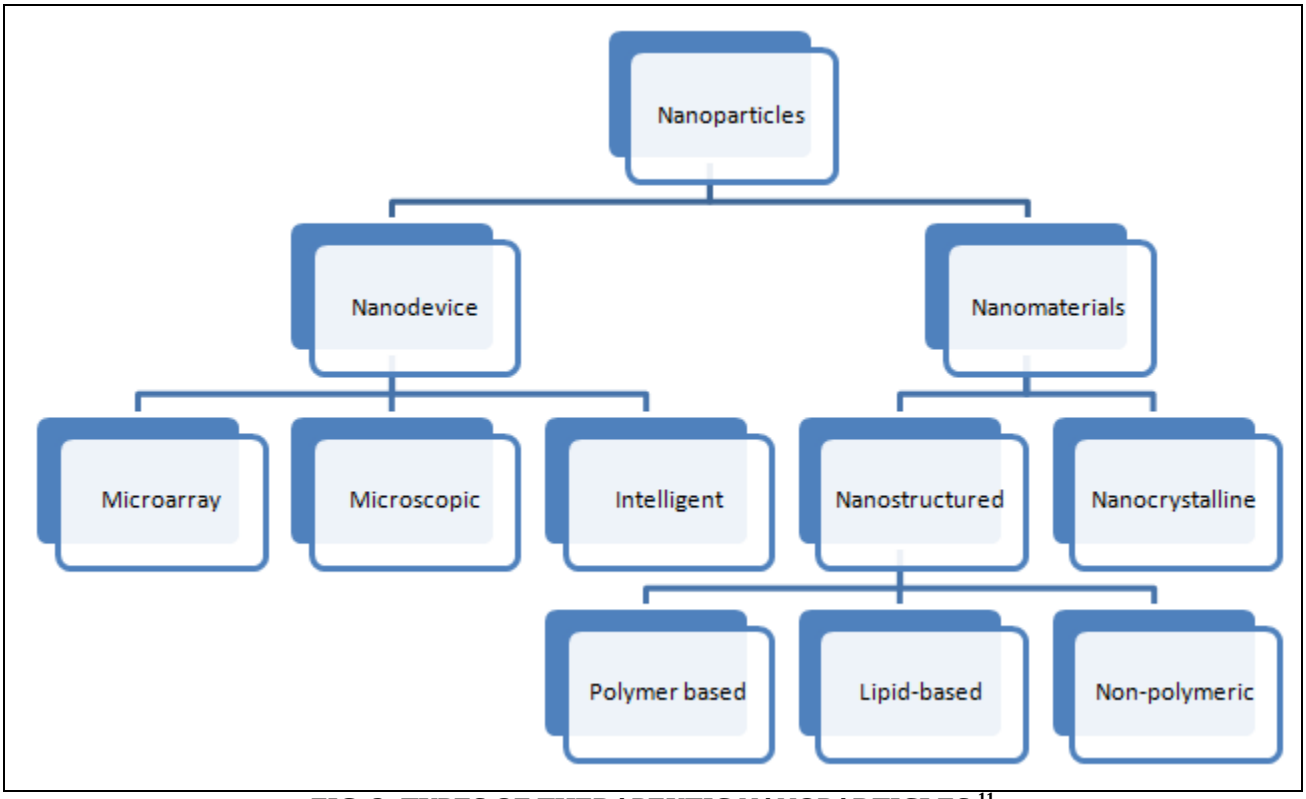

FIG. 3: TYPES OF THERAPEUTIC NANOPARTICLES [11]

Preparation of Nanoparticles: Nanoparticles are produced from various types of materials like protein, polysaccharides, metals & synthetic materials. The selection depends on various factors like:

- Size
- Solubility and Stability
- Charge and permeability of particle surface
- Degree of biocompatibility, biodegradability and toxicity
- Drug release ability
- Antigenicity of product formed

Nanoparticles Preparation Method:

Dispersion of Preformed Polymers: In this method by using polylactic acid (PLA), poly (D, L glycoside), PLGA, PLG, and Polycyanoacrylates biodegradable Nanoparticles are prepared. The use of biodegradable polymers minimizes toxicity [12].

Solvent Evaporation Method: In this process in an organic solvent like ethyl acetate, chloroform, dichloromethane, polymers are dissolved. After this in preformed polymers drug is dissolved. Then, emulsifier and surfactant in an aqueous solution are emulsified to prepare o/w emulsion [1]. Using an unceasing stirrer, the stable emulsion is formed, and the solvent should be evaporated by reducing pressure. Ultra-sonification and homogenizer are used to form a small uniform particle size of NPs [14]. It was the first developed method used to obtain polymeric NPs [15] **Fig. 4.**

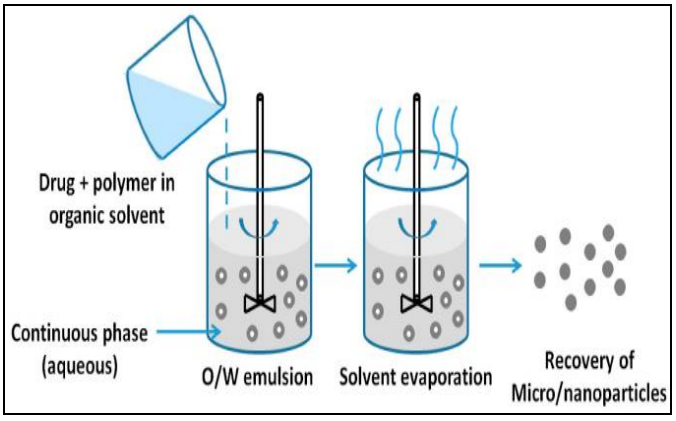

FIG. 4: REPRESENTATION OF SOLVENT EVAPORATION

Solvent Diffusion or Spontaneous Emulsification Method: It utilises water-miscible solvent and immiscible solvent. The extempore diffusion gives rise to interfacial turbulence between both phases and forms minute particles. An increase in the water-miscible solvent concentration may decrease

particles. The method can be applied for both hydrophilic and hydrophobic drugs [12]. This method has many advantages, like more than 70% encapsulation efficiency, simplicity, high reproducibility, and narrow size distribution [13] **Fig. 5.**

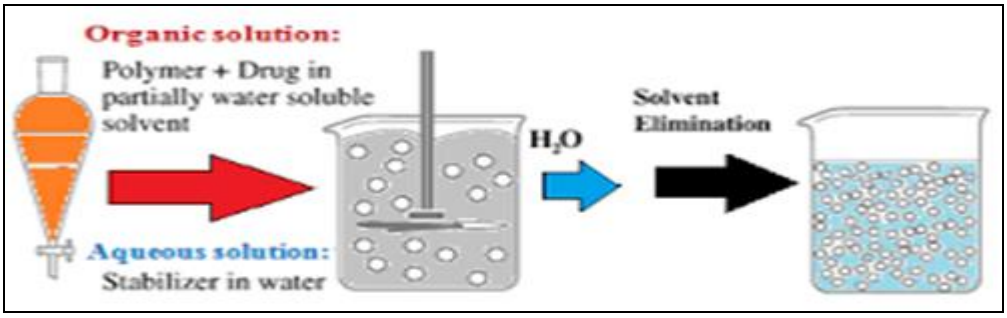

FIG. 5: REPRESENTATION OF SOLVENT DIFFUSION METHOD

Polymerization Method: In this technique, Nanoparticles are formed by polymerizing monomers; in an aqueous solution drug is added by adsorption after polymerization is completed. Ultracentrifugation is used to purify the Nanoparticles suspension and remove the stabilizers and surfactants [12] **Fig. 6.**

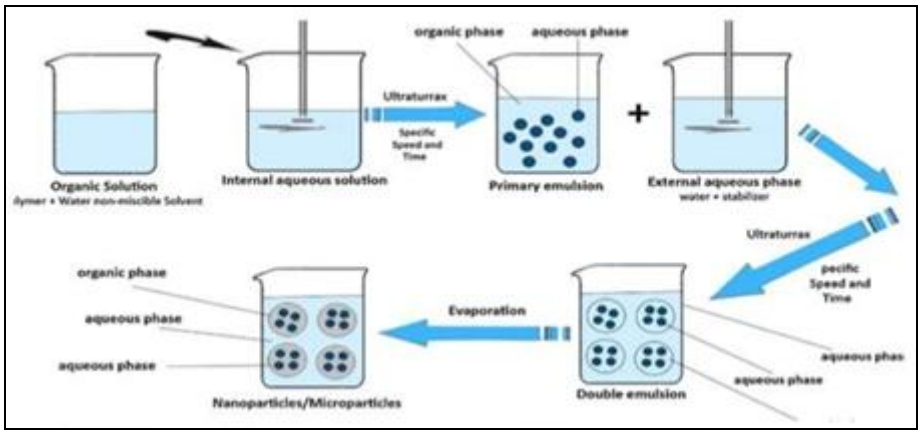

FIG. 6: REPRESENTATION OF POLYMERIZATION METHOD

Ionic Gelation or Coacervation Method: This technique involves the mixture of two aqueous phases

- ❖ The chitosan polymer, propylene oxide and a di-block copolymer ethylene oxide
- ❖ Polyanion sodium tri-polyphosphate.

The positively charged amino group of chitosan interacts with negatively charged tri-polyphosphate to transit it from liquid into gel form because of ionic interaction [16] **Fig. 7.**

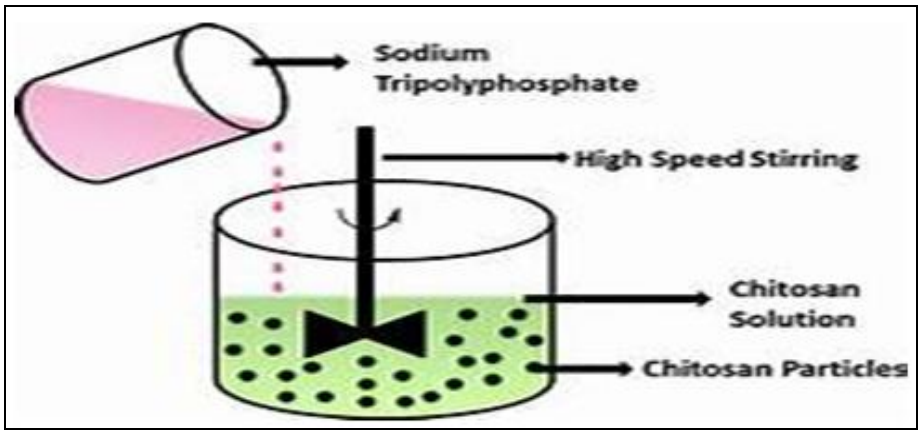

FIG. 7: REPRESENTATION OF IONIC GELATION METHOD

Supercritical Fluid Technology: This technique involves the absence of organic solvent, which is toxic for the environment and humans. Supercritical fluids are environmentally safe [13]. The techniques used for preparation with supercritical fluids are rapid expansion of critical solution and supercritical antisolvent. For the SAS technique, the organic solvent is mixed with supercritical fluid by which precipitation occurs, and Nanoparticles are formed. RESS process produces polymeric Nanoparticles product [16] **Fig. 8.**

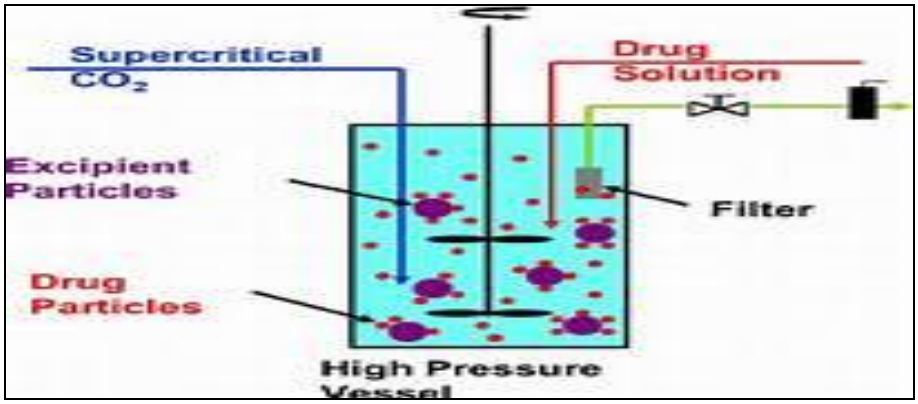

FIG. 8: REPRESENTATION OF SUPERCRITICAL FLUID TECHNOLOGY

Characterization of NPs: The NPs are characterized according to its size, surface charge and morphology. There are various advanced techniques to define the nature and size of Nanoparticles **Table 1.**

TABLE 1: VARIOUS TECHNIQUES & TOOLS FOR CHARACTERIZING NANOPARTICLES ARE LISTED [17]

Parameter	Method
Carrier-drug interaction	Differential scanning calorimetric
Charge determination	Zeta potentiometer
Chemical analysis of surface	Ion mass spectrometry
Drug stability	Bioassay of drug
Particle size	SEM, TEM
Release profile	*In-vivo* determination
Surface hydrophobicity	x-ray photoelectron microscopy

Evaluation Parameter of NPs:

The Yield of NPs: It is calculated by the overall weight of Nanoparticles divided by the total weight of drug in Nanoparticles with polymer [16].

% yield = amount of Nanoparticles / amount of drug + polymer x 100

Drug Entrapment: This is determined with HPLC by ultracentrifuge [16].

% drug entrapment = W-w / W x 100

Stability of Nanoparticles: To determine the stability of NP's store Nanoparticles preparation at 4°C ± 1°C and 30°C ± 2°C on stability chamber [18].

Particle size: For Nanoparticles evaluations, particle size and morphology are essential characteristics. Drug targeting and drug release are the two most significant applications of Nanoparticles drug delivery. Drug release is depending upon the particle size. The smaller size of Nanoparticles may aggregate during transportation and storage. So, there may be a compromise between stability and the small size of Nanoparticles. Particle size also affects the degradation of the polymer. Particle size was determined by Nano ZS90 zeta sizer, the zeta potential was also measured with the same zeta sizer [19].

DLS (Dynamic Light Scattering): It is one of the most popular methods to examine particle size [20]. It is used to examine the Brownian NPs in colloidal suspension. When the laser hits the moving particles which are in Brownian motion it causes the Doppler shift and change of wavelength. The change is related to Nanoparticles size [21]. For DLS analysis, the 3ml suspension of Nanoparticles and instrument Nano ZS was used [22].

SEM (Scanning Electron Microscopy): It gives the morphological examination via direct visualization. The Nanoparticles solution was prior converted into dry powder for SEM examination then the powder was placed on the sample holder and coated with a conductive meta [23]. Some literature reveals that SEM is found more

appropriate for metallic Nanoparticles than polymeric and oxide-based Nanoparticles, and SEM is also appropriate for Nanoparticles having a size more than 50nm [25].

TEM (Transmission Emission Microscopy): The preparation of sample is complicated and time taking in TEM because sample is needed to be ultra-thin. The sample is deposited to the support grid or films. The surface characteristics are obtained after the electron beam is passed through an ultra-thin sample of nanoparticle [24].

Zeta Potential: Nanoparticles interact with the environment and determining its electrostatic interaction with the bioactive compounds is very important depending on the nature and intensity of the surface charge determined by zeta potential [26]. The surface charge correlates to a potential difference of shear surface to the outside Helmholtz plane [27]. Either negative or positive values of zeta potential ensured the Nanoparticles stability and provided the nature of coated material. The zeta sizer HS3000 is used to analyse zeta potential [28].

Application of Nanoparticles:

Cancer: Developments in Nano-delivery system have enabled therapeutic agents to directly target the cancer cells at controlled rate with better efficacy [29]. Drug conjugates are directly accumulated around tumor cells which decrease the systemic toxicity of drugs

Infectious Diseases: Majority of infectious disease are treated with anti-microbial drugs which have major issue of drug resistance, dose toxicity. Nano medicine has promised applicability in combating this limitation and be useful against bacteria, viruses, fungus, or parasites [30].

Autoimmune Diseases: Rheumatoid arthritis and AIDS are major immunological diseases which has employed this approach. The new therapy approach directly targets the synovial membrane to prevent systemic and undesirable effects as well as decrease bone resorption and destruction[31].

In Food Industry: By nanotechnology food production should be improved for food processing and food packaging the nanotechnology is used in many industries. Nano composites directly release anti-microbial agents with the help of coating material in the food packaging [32]. Nano drops are used in canola oil industries as an additive to introduce minerals and vitamins in food.

Nanoparticles as DDS: Delivery system aims to discharge the payloads at diseased tissue through active and passive targeting. Passive targeting takes the carrier to infected tissue and active targeting relies on specific recognition of ligand[33]. Engineered nanomaterials have a significant role in improving disease diagnosis and specific treatment. Nanotechnology helps us get over limitation over conventional delivery like biodistribution, intracellular trafficking through - cell selective targeting, molecular transport to particular targeted organelles. Nanoparticles improve the stability and solubility of encapsulated drug, facilitate its transport through membrane and enhance circulation period to improve safety and efficacy [34].

COVID-19- Nanoparticles mRNA a lipid vaccine was authorized by FDA in the year 2020 as under emergency use authorization for COVID-19 [35].

Nanoparticles Toxicity: At present, diseases like cancer and autoimmune diseases are diagnosed and treated using nanoparticles [36]. The term Nanotoxicity originated in 2004, which defines the study of toxic effects on the biological and environmental system caused by the nanoparticles [37].

Nanotechnologies followed to improve the potential and minimize the side effect of the drugs on the human body. Toxicity is still a significant concern for the preparation of Nanoparticles formulations. For example, in March 2006, over 110 consumers in Europe pulled their product after reporting respiratory symptoms, so this should be a need to discuss nanotechnologies and toxicity. Symptoms like dermal change, cardiac toxicity, sensitization, neurotoxicity, and growth toxicity are caused due to the decomposition of Nanoparticles. Biodegradable polymers like PLA, PGA, and PLGA are used to minimize toxicity [38].

However, all the biodegradable polymer is not safe to use in humans. FDA regulates the GMP (Good manufacturing practice) protocols for the medical use of PLA and PLGA, ensuring safety, efficacy, and stability [39].

It is one of the fastest-growing fields of research, and in the future, more biodegradable Nanoparticles will be formulated for clinical and medical uses. Various ongoing research shows that Nanoparticles have the ability to accumulate in the body cells that will lead to organ specific toxic reactions. So, the impact of Nanoparticles on body cells must be thoroughly investigated and addressed before its therapeutic utilization [40].

Future Prospective: Nanotechnology is a booming research area because of to vast area of utilization but the biggest challenge is to reduce its organ specific toxicity due to accumulation in various body cells. To create safe, effective and economical Nanoparticles synthesis of Nanoparticles from biodegradable waste is on trend which will also help us in waste management. Still, we need to thoroughly investigate the impact of NPs on body cells [41, 42].

CONCLUSION: The application of nanotechnology is an incentive for emerging technologies for maintaining/improving human health. It involves three kinds of chemical behaviour, separation, deformation, and consolidation. NPs are an excellent choice for the treatment and diagnosis of diseases.

Various preparation methods such as solvent diffusion, polymerization of monomers, solvent evaporation, ionic gelation, and supercritical fluid technology are used to achieve Nanoparticles and various biodegradable polymers (PLA, PGA, and PLGA) are used to minimize toxicity. This review is related to the Nanoparticles preparation method, evaluation parameter classification, toxicity, and application. This review concluded that nanoscience leads to a revolutionary change in the area of world medicines.

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