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Review on Polymer Based Nanoparticles for Increase the Bioavalibilty of Poorly Water Soluble Drug

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

In this review study about the polymeric nanoparticles and how polymer based nanoparticles increase bioavailability of less water soluble drugs. Polymeric nanoparticles have a matrix of biodegradable and biocompatible polymers of synthetic and natural origin. Polymer based nanoparticles are very useful for increase the solubility of the poor water-soluble drugs by decrease the particles size. Polymeric nanoparticles are very useful for targeting the drug to the specific site. Polymeric nanoparticles are also used to maintain and control the release of the drug. In present review study on the type of polymer used for the preparation of the polymer based nanoparticles. The choice of method depends on a number of factors, such as, particles size, area of application and characterization of polymeric nanoparticles.

Keywords: Nanosphere or Nano capsules; natural and synthetic polymer; solvent evaporation method; zeta potential.

1. INTRODUCTION

Nanotechnology is the advanced technology used in the research area. In this technology impressive development in the medical field and used various technology for formulate the nanoparticles with according to requirement [1]. For preparing the polymeric nanoparticles the

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material are used to enhance the physiochemical features of the drug. Due to Nano size of nanoparticles, nanoparticles the surface area larger than macro-sized material. Nanotechnology used in the developments in the field of biosensor, biomedicine and bio Nano technology [2].

2. CHALLENGES COME IN ORAL DRUG DELIVERY SYSTEM

Various factors that are affect oral drug delivery system. Oral drug delivery system are suitable for drugs with greater water solubility and permeability. But now a day most new compounds are currently lipophilic and therefore low water solubility [3]. A number of new therapeutically active bodies are characterised by the BCS classification system. BCS class 2 (low water solubility and high permeability) and BCS class 4(low water solubility and low permeability) drug have low water solubility and number of barriers are present in GIT which are reduce the pharmacological effect of the drug. Various enzymes present in the GIT and pH of the GIT also affect the bioavailability of the drug. Due to change in the pH and presence of the enzyme in the GIT influence the oral bioavailability of many drugs [4].

Various Reasons for poor oral bioavailability of water insoluble drugs

- Poor aqueous solubility
- Degradation in GIT track
- First pass metabolism
- Insufficient time for absorption
- Inappropriate partition coefficient
- Insufficient time for absorption

To overcome these problems nanotechnology are developed. In present review study about polymeric nanoparticles used to enhance oral bioavailability of the less water soluble drug by using many type of polymer or study the different method used for preparation of the polymer based nanoparticles [5].

3. POLYMER BASED NANOPARTICLES

The solid colloidal particles are come 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]

Types of Polymeric nanoparticles are

Nanosphere
Nanocapsule

Nano capsules

Nano capsule are the reservoir systems. In this system drug is entrapped in unique polymer membrane.

Nanosphere

Nanosphere is matrix systems. In this system drug is dispersed in polymeric matrix [6].

For preparation of polymer based nanoparticles two main strategies are used such as

- Top-down approach
- Bottom-up approach.

In top-down approach polymeric nanoparticles are developed by dispersion of the polymer.

In the bottom-up approach polymer-based nanoparticles are developed by polymerization of monomers.

Selection of the suitable method used for the preparation of the polymeric nanoparticles depend on the various factors, such as

- Particle size of drug
- Type of solvent
- Type of Polymer
- Application area

Monomer used in Molecular inclusion as their starting point for "bottom-up" process to formulate polymer-based nanoparticles.

Advantages

- Polymer based Nanoparticles are more effective for targeting drug in specific site.
- Polymer based nanoparticles are useful for controlled and sustained release of the drug.
- It is helpful to increase the stability of any volatile agents.
- It has more benefits in term of quality than conventional oral methods of administration.
- The choice of polymer and their ability to regulate release of medicine from polymer-based nanoparticles have made it suitable for cancer treatment, vaccine delivery, contraception and supply of selective antibiotics.

4. POLYMER USED FOR PREPARATION OF POLYMERIC NANOPARTICLES

Polymer: Polymers can be found naturally in plants and animals (natural polymers) or they can be man-made (synthetic polymers). Polymers offer a variety of unique physical and chemical qualities that allow them to be used in everyday life. Natural, synthetic, and semi-synthetic polymers are the three types of polymers included in this category.

4.1 Classification of Polymer

Based on Origin:

Polymers derived from nature:

They are present in both plants and animals and exist naturally. Proteins, starch, cellulose, and rubber, are the example.

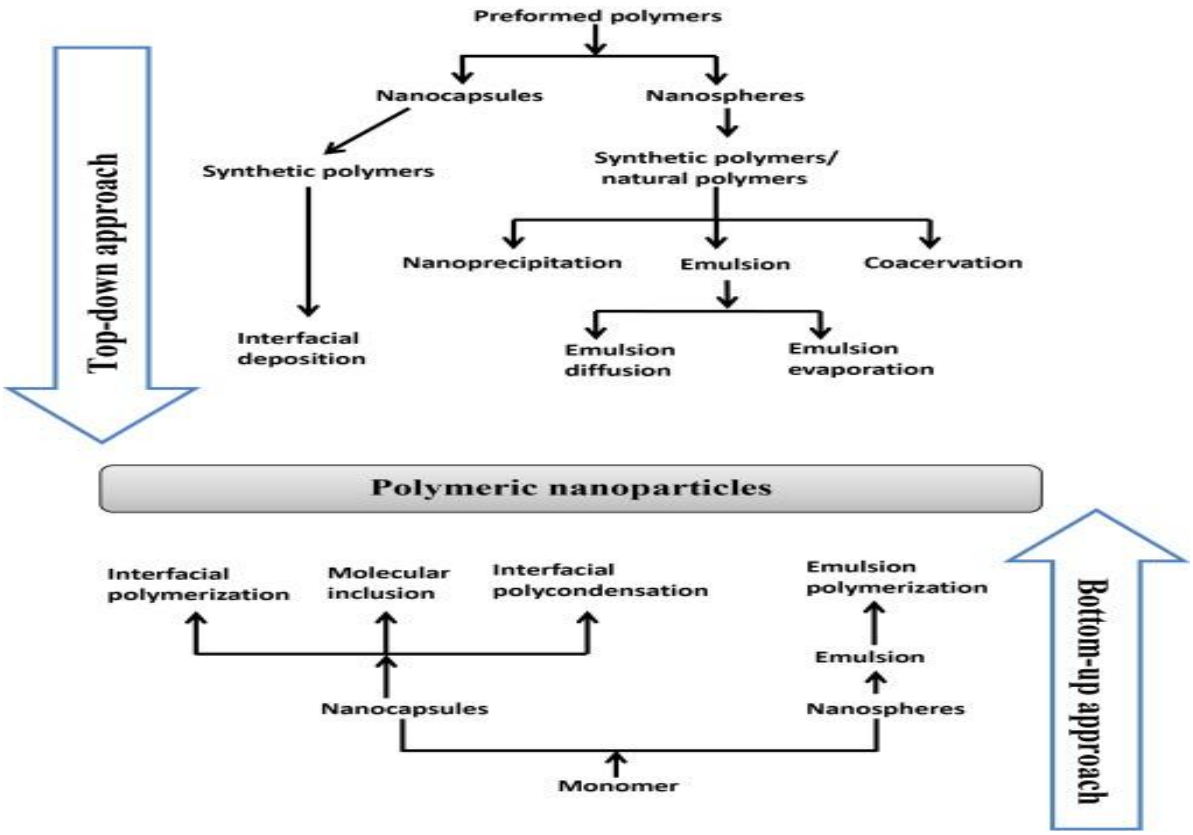

Fig. 1. Explain Top-down approach and Bottom-up approach

Table 1. Classification of the Polymeric ingredients used for development of the polymeric nanoparticles

Material	Full name	Abbreviation/common name
Synthetic homo polymer	Poly (lactide) Poly (lactide-co-glycolide) Poly (epsilon-caprolactone) Poly (isobutyl cyanoacrylate) Poly(isohexylcyanoacrylate) Poly (n-butyl cyanoacrylate) Poly (acrylate) Poly (methacrylate)	PLA PLGA PCL PICBA PIHCA PBCA Eudragit*
Natural polymer	Chitosan Alginate Gelatin Albumin	
Copolymer	Poly (lactide)- poly (ethylene glycol) Poly (lactide-co-glycolide)- poly (ethylene glycol) Poly (epsilon-caprolactone)- poly (ethylene glycol) Poly (hexadecyl cyanoacrylate-co-poly (ethylene glycol) cyanoacrylate)	PLA- PEG PLGA-PEG PCL-PEG Poly (HDCA-PEGCA)
Colloid stabilizer	Dextran Pluronic F68 Poly (vinyl alcohol) Co polymers (see above) Tween®20 and Tween® 80	F68 PVA

Polymers that is semi-synthetic:

They are made from naturally existing polymers that have been chemically modified. Cellulose nitrate and cellulose acetate are example of semi synthetic polymer.

- Synthetic fibers: The fibers obtained by polymerization of simple chemical molecules in laboratory are synthetic fibers. e g. Nylon, terylene, polyethene, polystyrene, synthetic rubber, nylon, pvc, backlite, Teflon, Orion etc.

The classifications based on the structure are three types of polymers as follows:

Linear polymers:

In these polymers monomers are linked with each other and form a long straight chain. These chains have no any side chains. e g. Polyethene, PVC, Nylons, polyesters etc. Their molecules are closely packed and have high density, tensile strength, and melting point.

Branched polymers:

They have a straight long chain with different side chains. Their molecules are irregularly packed hence they have low density, tensile strength and melting point, e g. polypropylene (side chain —CH3), amylopectin and glycogen.

Network or cross-linked polymers:

These monomeric units are linked together to constitute a three-dimensional network. The links involved are called cross links. They are hard, rigid and brittle due to their network structure, e g. Bakelite, Melamine, formaldehyde resins, vulcanized rubber etc.

The classification based on molecular forces:

Mechanical properties of polymers like tensile strength, toughness, elasticity depends upon intermolecular forces like van-der Waals forces and hydrogen bonding. On the basis of these forces they are classified as.

Elastomers:

These are the polymers in which polymer chains are held up by weakest attractive forces. They contains randomly coiled molecular chains having few cross links. As the stain is applied polymer get stretched and as the force is released polymer regain its original position. These polymers are elastic and called elastomers, e.g. Neoprene, and vulcanized rubber.

Fibers: They have high intermolecular attractive force like Hbonding. They have high tensile strength and used in textile industries, e g. Nylon-6, Nylon-66, and Terylene.

Thermoplastic polymers: These are the polymers having intermolecular forces between elastomers and fibers. They are easily molded in desired shapes by heating and subsequent cooling at room temperature. They may be linear or branched chain polymers. They are soft in hot and hard on coding, e g. Polythene, polystyrene, PVC.

Thermosetting polymers: This polymer is hard and infusible on heating. These are not soft on heating under pressure and they are not remoulded. These are cross linked polymers and are not reused, e g. Bakelite.

The classifications based on polymerization process are two types as follows:

Addition polymers: The polymers formed by the addition of monomers repeatedly without removal of by products are called addition polymers. These polymers contain all the atoms of monomers hence they are integral multiple of monomer unit, e g. Orion, Teflon, polyethene, polypropylene, PVC. The monomeric units are generally alkenes and its derivatives.

Condensation polymers:

They are formed by the combination of two monomers by removal of small molecules like water, alcohol or NH3. They have ester and amide linkage in their molecules. Their molecular mass is not the integral multiple of monomer units, e g. Polyamides (Nylons), polyesters, polyurethanes [8].

5. METHOD USED FOR PREPARATION OF POLYMER BASED NANOPARTICLES ACCORDING TO TYPE OF POLYMER BASED NANOPARTICLES

Methods used for the preparation of the polymer-based nanoparticles according to the type of drug and rout of drug administration. For the processing of the particles various type of method is used, mainly two strategies are such as

- Diffusion of performed polymer
- Polymerization of monomers

In all methods use performing polymers and organic solvent used for firstly dissolve the polymer. But organic solvent produces toxic

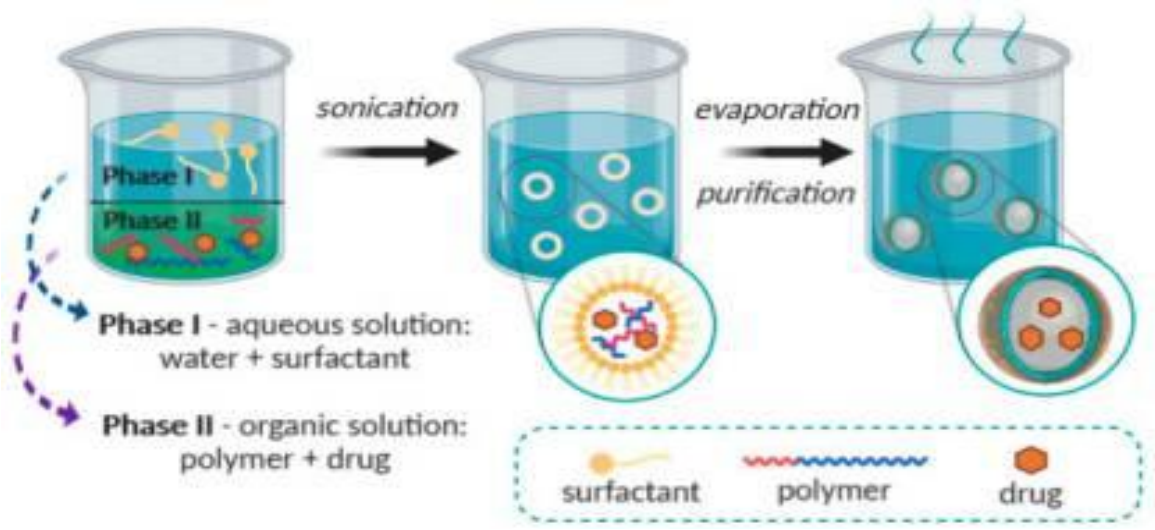

Fig. 2. Graphical representation of solvent evaporation method

effect and environment risk. So, the solvent residue removes for the final product. When the drug loads to the polymeric nanoparticles, methods depend on the polymerization of the monomer and permit the addition with larger effectiveness and in one single step. Method of preparation not employed carefully then the product is converted to the aqueous colloidal suspension.

5.1 Nano Spheres

- Solvent evaporation method
- Solvent diffusion
- Nano precipitation
- Reverse salting out

5.2 Nanocapsule

- Nano precipitation

5.3 Solvent Evaporation

The oldest process used for polymeric nanoparticles preparation was solvent evaporation. Nanoparticles made from the performed polymer in this process. In this method firstly prepare oil with the water emulsion form (O/W).After that prepare nanosphere [9,10].

5.4 Steps Involved in Solvent Evaporation

- Prepared organic phase by the use of the polar organic solvent polymer are dissolved in this solvent.
- After that add the drug by dissolution or dispersion.
- Acetone used as a solvent [11].
- But they are toxic so they are replaced by ethyl acetate [12].
- Ethyl acetate show better toxicological profile so they are used biomedical applications [13].
- Aqueous phase prepared with the surfactant such as polyvinyl acetate(PVA) [12]
- Add drop by drop organic phase in aqueous phase
- This emulsion has been split into nanodroplets by applying exterior energy during sonication.
- For remove the solvent by evaporating the solvent by magnetic stirring at 300 rpm under atmospheric condition for 2 hours [14].
- After removing the solvent lyophilization done for dry the liquid sample

5.5 Solvent Diffusion

- This method is modification method of the emulsification / reverse salt process.
- This technique, first prepare an oil in water type emulsion of the polymer and drug with water soluble solvent and aqueous solution with a surfactant [15,16]. In this type emulsion the internal phase consists the hydro-organic solvent and this solvent saturated with water and both phases are thermodynamically equilibrium of the two phases at room temperature [17].
- When dilution done with the great amount of the water, after diffusion of solvent colloidal particles, diffuse the solvent from the dispersed droplets to external phase after diffusion of the solvent colloidal particles are formed.
- Nan sphere are formed by this method and Nano capsules can also be formulated by this method but if the small amount of oil.
- In final step boiling of the organic solvent are avoided by evaporation and filtration [18]. After filtration and evaporation nanoparticles are obtained dimensions range from 80 to 900 nm.
- In current study this technology is used for the development of the polymeric nanoparticles by use of high volume of aqueous phase. And risk of diffusion of the hydrophilic drug into aqueous phase are avoided by must be removed from the colloidal dispersion [19,20].

5.6 Reverse Salting-Out

- In this technique water soluble solvent are separate from an aqueous solution by salting out effect so this method is useful for the development of the nanosphere [21]
- In this process O / W emulsion composition is different because the water-mixable polymers solvent are used.
- Add salting out agent and colloidal stabilizer in aqueous phase [22].
- Salting out agents are
  - Magnesium chloride ($MgCl_2$)
  - Calcium chloride ($CaCl_2$)
  - Magnesium acetate (Mg $(CH3COO)_2$)
  - Non-electrolytes, e.g., sucrose [23].
- Acetone and water miscibility are decrease by aqueous phase saturation that permits

an O/W emulsion are formed from the other miscible phase [24].

- O/W type emulsion produced by intense agitation at room temperature.
- After that emulsion was diluted to permit for dispersion of organic solvent in other stage by a suitable voltage of deionized water or an aqueous solution.
- The precipitating polymer and therefore production of nanosphere.
- The remaining solvent and salting agent is separated by filtration.
- The condition is not required but simplify the execution process between organic solvent and water [21,25].
- The dimensions of nanosphere obtained with this technique range from 170 to 1000 nm.
- Standard size can be modified between 200 and 500 nm by adjusting the inner phase polymer concentration /outer phase length [26].

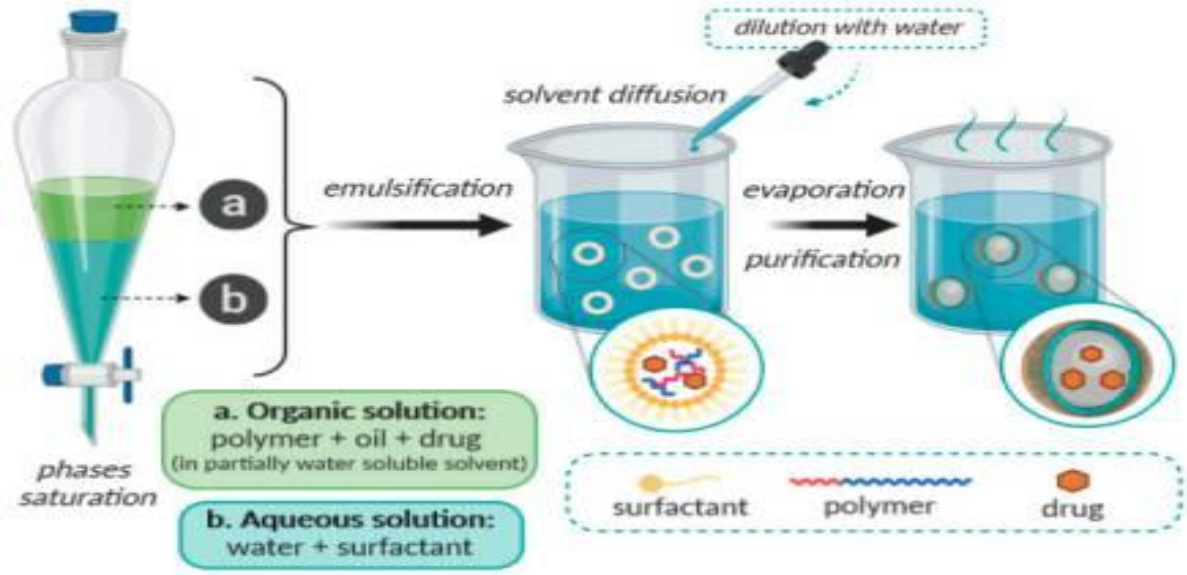

Fig. 3. Graphical representation of solvent diffusion method

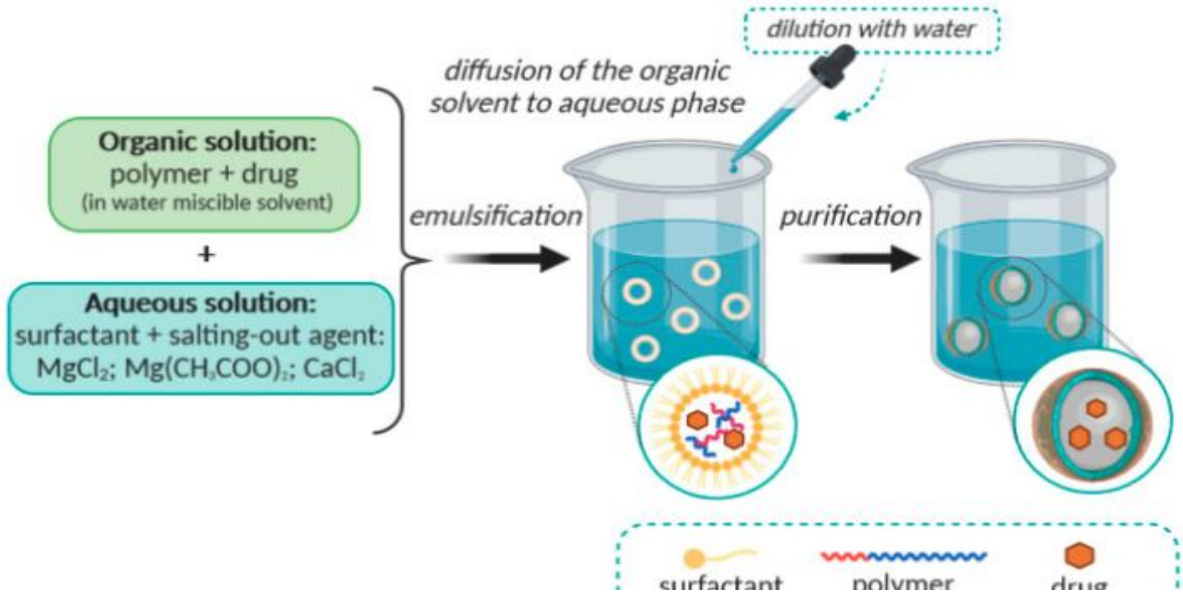

Fig. 4. Graphical representation of reverse salting out method

5.7 Nano Precipitation

- In this approach two miscible solvent are required, this approach is also known as solvent displacement method.
- Acetone or acetonitrile are a mixable organic solvent and polymer dissolve in this solvent [27–31].
- They are easily removed by the evaporation due to the insolubility with water [32].
- The polymer dissolved in water-soluble polarity solvent and this solution has to applied with continue stirring by controlled rate in an aqueous solution.
- Nanoparticles are obtained after the diffusion of the polymer in aqueous phase [32].
- When solvent dispersed from the Nano droplets then Nano capsule and nanosphere are formed in the form of polymer precipitates [33]
- In the phase, Surfactants may be used to make sure the stability of colloidal suspension, but existence of the surfactant is not needed to confirm the production of nanoparticles.
- Nanoparticles are getting by this technique they are usually described in definite size and small size distribution.
- This method is very good method as compare to other evaporation technique of the emulsifying solvent [34]
- In current study Nano precipitation is extremely helpful method for formation of polymeric nanoparticles in size range 170 nm in size [35]
- This method is used for the formation of nanosphere or Nano capsules [35]

5.8 Characterization of Polymer Based Nanoparticles

Physical properties of polymer based nanoparticles are different such as

- Arrangement
- Strength
- Size
- Shape
- Surface properties
- Crystallinity
- Dispersion state.

They are the most commonly used method [36,37]

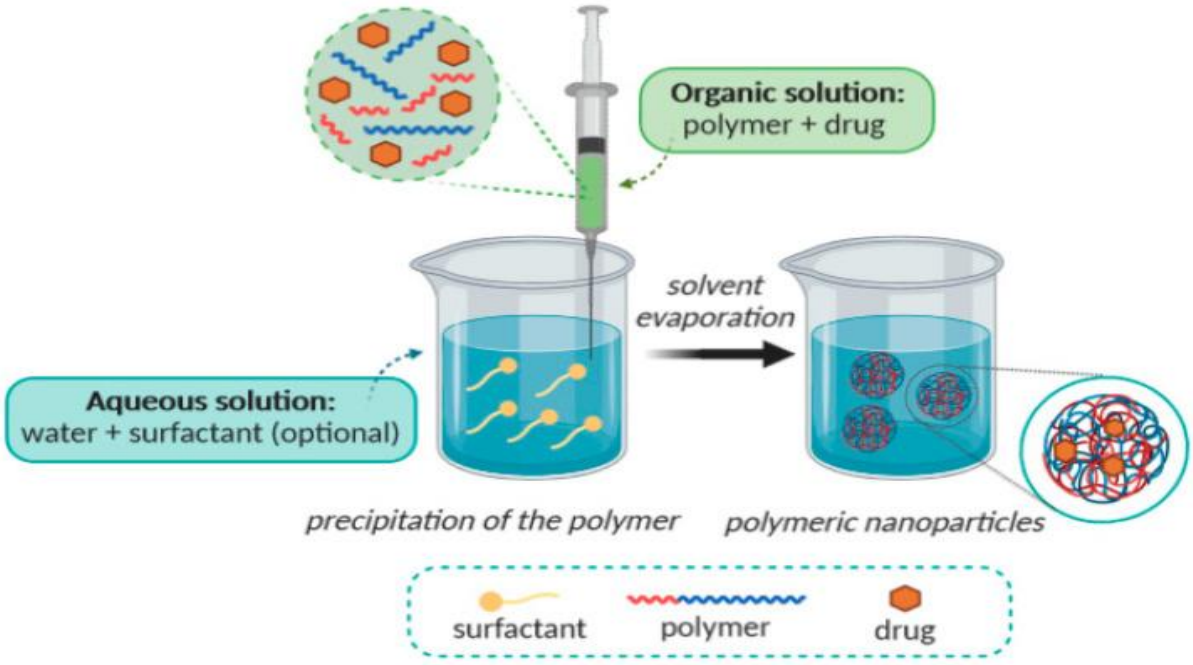

Fig. 5. Graphical representation of Nanoprecipitation method

5.9 Particle Size Distribution

- Different techniques are used for development of the polymeric nanoparticles in different particle size range.
- Particles diameters ranging between 60 to 70 nm [38]
- Nanoparticles size can be considered using many approaches for example:
    - Dynamic light scattering (DLS)
    - Static light scattering (SLS),
    - TEM, SEM and AFM [39]
    - For example, electron microscopy produces an image of particle separated from surrounding areas, while DLS enables hydrodynamic radius of suspended particles to be determined volume measurements can differ based on the process used.
    - In addition , DLS is main accompaniment to TEM because it can calculate more volumes by detecting changes in the distribution of particles size by providing information about the aggregation in solution [39,40].

5.10 Polymer Molar Mass Distribution

Molar mass distribution of polymer is studied behind the preparation this method helpful for study effect of formulation component on polymerization method and chemical reaction between drug and polymer information about the degradation of polymer [41]

- Size -exclusion chromatography is common technique used for study the polymer mass distribution. [42]
- The strength of light extend by polymeric NPs are analyzed by static light scattering [40]

5.11 Surface Area and Chemistry

- Various methods measure various surface aspects. Direct measurement of surface area of nanoparticles uses adsorption to create single layer of gas coverage like N2 under varied pressure
- The total surface area is the total area in relation to number of gas molecules essential to form a single layer as well as cross-sectional region of gas molecule absorbed [43]

5.12 Zeta Potential

Zeta potential is useful for study surface charge between particles. Zeta potential of polymeric nanoparticles is useful for study surface charge of nanoparticles. They are produced electrical potential in particles and is affected by arrangement of nanoparticles and the medium in which itself-dispersed [44]. If the zeta potential reaches (+/-) 30 mV then the suspension means that surface charge prevent accumulation of the particles [45]. The suspension is stable because surface charge prevents aggregation of particles. Zeta potential is useful in deciding loaded active material is encapsulated or adsorbed on surface inside Nanocapsule center. Zeta sizer provides full sensitivity, precision and zeta potential resolution ever. Also very low mobility can be evaluated and distributions of mobility measured.

- Stability of emulsion
- Stability of formulation
- Pigment functioning
- To determine the Impurity

Table 2. The zeta potential limits for colloids in water

Stability	Range Unit (mV)
Fast clotting or flocculation	0 to ±5
Volatility Incipient	±10 to ±30
Mild stability	±30 to ±40
Good stability	±40 to ±60
Excellent stability	Over ±60

Potentiality of the zeta represents the surface load of the particles due to changes in interface with dispersing medium breakdown of functional groups on surface of particles and ionic adsorption there in aquatic medium and solvent effect [44] the zeta potential is determined from electrophoretical movability of particles in their respective solvent [45–47].

5.13 Suspensions pH

The pH can be tracked as a function of the time to obtained relevant information on nanoparticles stability. The pH shift, For example, can show a deterioration of polymers suggesting changes in protons on the surface of the particles. Decrease of Molar mass confirmed after 6 months of storage in Nanocapsule and Nanocapsule suspension with the resulting decrease in pH .However, in the short period of time, the

decrease in the pH of the suspensions may be due, depending on polymeric water power to carboxylic groups in polymer and release of protons in surrounding medium. Furthermore, the pH of the medium may have an effect on zeta potential and electrostatic stability of solution, and monitoring it is of great importance [18].

5.14 Stability of Polymeric NPs Suspensions

- Various physiological parameters are important for stability of polymer based nanoparticles [48].
- In these nanoparticles, concentrated solution of medicines and adsorption phenomena are preserve due to problems of low physiochemical stability and longer storage periods [49].
- The principle limitations include the aggregation of particles, the chemical stability of the polymer. Furthermore, the need to add preservative in Oder to postpone or to prevent such physicochemical and micro biological problem typically involves the drying process [50].
- In Freeze-drying removing of water by sublimation, generally used for drying nanosphere, while spray drying is an alternative to lyophilizing, in Oder to improve stability of solid lipid nanoparticles, it consists of transferring the solution into drying chamber through an orifice of atomized atom, with hot counter-current or mixed air co-flow, which favors the quick droplet drying. [51]
- The separated and collect dry solid particles are formed in form powder, granules and agglomerates [52,53].

6. STUDY ABOUT THE DRUG ASSOCIATION

Study about the quantity of active ingredient related with nanoparticles is especially difficult due to its small size, which make it hard to distinguish active ingredient from the relevant fraction [54] Ultracentrifugation is well used system of separation, where free drug in suspension is calculated after centrifugation. Dissolution is helpful for determine total drug concentration is typically determined into an acceptable solvent of a fraction of the nanoparticles. The nanoparticles active substance concentration is then determined difference between the total concentration and free active substance concentration [55,56] he ultra filtration centrifugation, where the membrane is used to isolate a section of aqueous phase from colloidal suspension, is also a tool that has been used. The free active ingredient concentration is estimated in the ultra filtrate, and also by subtract total and free levels of the active substance fraction associated with the nanostructure [55].

- Various factors can influence the amount of drug in nanostructure systems according to published studies such as:
  - ❖ The drugs Physiochemical properties
  - ❖ The medium pH value
  - ❖ Properties of the NP surface or type of polymer,
  - ❖ The Amount of drugs used in the formulation, [57,58]
- It is possible to get unlike drug association rates with the same initial drug concentration by changing particle surface properties, via adsorption.
- In determining capability to extend the drug action time, this parameter is very important.
- The adsorption isotherm on the surface of nanoparticles should also be calculated, since it offers details about the distribution of the material on the surfaces of the particles and how related power is the drug has different type of nanosphere interaction [58] the drug has different type of nanosphere interaction, which can be dissolving or dispersed in polymer matrix or adsorbed on polymer.
- Nanocapsule is developed to improve the loading of lipophilic active substances that should be found in an oily core polymer membrane dissolved.
- Since then it is also becoming a complex method to evaluate the mode of associated with nanoparticles is determined by the available method.
- Therefore only comparable studies of the capacity of zeta potential, release profile, division of the molar mass, studies of adsorption, and rate of drug association with nanostructures [59]

7. PHARMACEUTICAL IN VITRO RELEASE KINETICS

Discharge of drugs from polymeric Nanopartilces is determined by following factors [60,61] Various experimental techniques for

determining kinetics in vitro release of a drug entangled in nanoparticles:

a) Artificial or biological membranes side by side diffusion cell
b) Dialysis bag distribution method
c) Reverse dialysis sac system
d) Ultracentrifugation
e) Ultra filtration
f) Centrifugal Ultra filtration method [62]

Release rate of entrapped medicine affected by different factors. Release of medicine depends on:

- Polymer based nanoparticles structure
- Polymer Type and length of polymer
- Degradation or erosion

The kinetics of nanosphere release from drug are typically exponential perhaps due to dispersion of drug from polymeric matrix to its surrounding atmosphere [60,63]. For Nano capsules the medicinal substance supposedly dissolved in oil nucleus will be released by diffusion Nano capsules and Nano emulsion related drug release profile suggested a polymeric surface of the Nanocapsule.

8. CHALLENGES IN RESEARCH IN NANOECOTOXICOLOGY

In 2008, a Behra and Krug publication in part on nature Nanotechnology identify three key issues that to need to solve these issues in few years [65]

- The selection of nanoparticles in experiments and biological tests for the identification of nanoparticles before, during and after the experiments it is important to determined the physical or chemical properties, aggregation and sedimentation ability.
- Manner in which species in various ecosystems accumulate synthetic nanoparticles must be investigated.
- Collection of species for use of experiments and measurement points.

9. *In vitro* AND *vivo* TOXICOLOGICAL STUDIES

This system has consisted of various advantages and they are providing stable formulation. In this type drug delivery system different active ingredient are encapsulated. But in this system nanotoxicity are produced and unexpected toxic effects are occurred. [67]. Toxological and response profile of the nanoparticles are proved in suitable animal modal. In this modal represent the pathophysiology of human disorder [68]. The main characteristics of the polymeric nanoparticles is Biocompatibility, biodegradability and non-toxicity [67,69,70]. Polymeric nanoparticles are useful for to improve the bioavailability and they are safe for human being. They are stable and contain the ability to encapsulate a number of substances. In current study biodegradable and non-biodegradable polymeric carriers are used for oral drug delivery system [71]. For example curcumin loaded polymeric nanoparticles used for oral drug delivery system are used they provide 5-6-fold more oral bioavailability than pure curcumin [71]. Polymeric nanogels have also been shown to show a minimal toxicity, serum stabilization and stimulus reactivity, as they are highly encapsulated, tunable size are obtained. So, the surface image of topical administration polystyrene NPs ex vivo studies have shown aggregation of NPs in the follicular openings, are commonly used in biomimetic material and biosensors, drug delivery, tissue engineering. [69,70]. The transdermal drug delivery system can assess the first pass metabolism effect thus less drug use can be effectively used with less toxicity [72]. Researcher spoke about biomimetic methods such as cell-membrane camouflage and the creation of stubborn Nano supply systems [73]. Polymeric NPs are difficult to use as chemotherapeutic systems as there is low circulation stability and targeting inefficiency. Biocompatible and biodegradable pH reactive hybrid NPs has been achieved to solve these problems. These Nano structure based on the PLGA nucleus, have been protected by a cross linked bovine serum albumin shell [74].

Presently, the effect of polymeric nanoparticles is important in medicine. So, it is very important clinical use of the drugs is controlled because the components are toxic in nature and polymers are used, they are biodegradable so they excrete by common metabolic pathways [75]. The toxic effect of the components is screened for study the toxicity [76].

9.1 Nanotechnology Used for Enhance the Bioavailability of Poorly Water Soluble Drug

The onset of action of water insoluble drugs are slow, less oral bioavailability, Drugs with low

Table 3. Example of polymer based nanoparticles preparation and method used for preparation

Type of polymer	Formulated drug/bioactive	Type of polymeric nanoparticles/method	Application	Reference
PCL, PLA, PLGA	Coumarin-6(C-6)	Nanospheres C-6-loaded polymeric core-shell NPs (polymeric core-multilayer polyelectrolyte shell NPs), obtained by prepared by the spontaneous emulsification solvent evaporation method	Drug delivery, theranostics and bioimaging	[78]
PLGA	Rapamycin	Rapamycin- loaded polysorbate 80-coated PLGA nanoparticles"	Anti-glioma activity	[79]
AcDex	Hyperforin	Hyperforin-loaded AcDex-based NPs formulated via single emulsion/solvent Evaporation using ethyl acetate and water	Anti -inflammatory	[80]
PLGA	Fenofibrate (Feno)	Nanospheres; PLGA-Feno NPs	Diabetic retinopathy, neovascular age-related macular degeneration (ocular neovascularization	[81]
Biopolymer of PCL	Amphotericin B (Amp B)	Nano capsules; PCL-NCs loaded with Amp B, obtained by nanoprecipitation method	Anti-leishmanial (Leishmania infections), anti-fungal	[82]
Anionic copolymer based on methacrylic acid and methyl 'methacrylate (EudragitL 100)	Fenofibrate (FF)	Nano capsules; FF-loaded-Eudragit L 100 NCs, obtained by nanoprecipitation method"	Undefined oral delivery	[83]
PLGA, PCL	Ciprofloxacin	Nano capsules; ciprofloxacin-loaded PLGA NCs, obtained by nanoprecipitation method	"In situ tissue regeneration and accelerated healing, anti-inflammatory activity"	[84]
PLGA	Curcumin (Cur)	Nano capsules; Cur-loaded PLGA NCs	"Antibacterial activity, pancreatic cancer"	[85,86]
F108: PEG-PPG-PEG	Curcumin (Cur)	Colloidal nano capsules; Cur-loaded PEG-PPG-PEG NCs	Anticancer	[87]
PEG	Pegademase	colloidal nano capsules;	Severe combined	[86,88]

Type of polymer	Formulated drug/bioactive	Type of polymeric nanoparticles/method	Application	Reference
	Bovine	Pegademase bovine-loaded PEG NCs	immunodeficiency disease	
PCL-PEG-PCL	Paclitaxel (PTX)	Nano capsules; PTX-loaded PCL-PEG-PCL NCs	lung cancers in combination with chrono-modulated chemotherapy	[89]
PLGA –PEG	Paclitaxel (PTX)	Nano capsules; PTX-loaded PLGA-PEG NCs	Breast, pancreatic andovarian and brain cancers	[89]
Eudragit® RS100, Eudragit® L100-55, Eudragit® EPO, PCL, polylactide, PLGA	Essential Oils	EO based-nanoparticles by nanoprecipitation method	Antioxidant/antimicrobial	[90]
PCL	Cymbopogon martini Roxb. (Palmarosa oil)	Nano capsules; Palmarosa oil-loaded PCL NCs	Antioxidant, antimicrobial	[91]
Eudragit® L100-55	Thymus vulgaris L. (Thyme oil)	Nano capsules; Thyme oil-loaded Eudragit® L100-55 NCs	Antioxidant	[92]
Eudragit®RS100	Citrus bergamia Risso (Bergamot oil)	Nano capsules; Bergamot oi-loaded Eudragit® RS100 NCs	Antimicrobial	[93]
Eudragit®RS100	Citrus sinensisL. (Orange oil)	Nano capsules; Orange oil-loaded Eudragit® RS100	Antimicrobial	[93]
Eudragit®EPO	Rosmarinus officinalis L. (Rosemary oil)	Nano capsules; Rosemary oil-loaded Eudragit® EPO NCs	Antioxidant	[94]
Eudragit®EPO	Lavandula dentata L. (Lavender oil)”	Nano capsules; Lavender oil-loaded Eudragit® EPO NCs	Antioxidant	[94]
PCL	Geraniol	Nano capsules; Geraniol-loaded PCL NCs	Antioxidant, antimicrobial	[91]

solubility, be short of dose proportionality, lack of stable plasma concentration, and unwanted side effects are studied. Due to poor water solubility result poor patient compliance The conventional dosage forms can therefore result in over or medication and poor patient compliance [77]. So, overcome these challenges by using novel drug delivery. In this review study about the polymeric nanoparticles and how prepare polymeric nanoparticles. PNs are useful for reduce the dose frequency; reduce the dose size, site specific targeting, enhanced permeability, and improvement in oral bioavailability. Polymeric nanoparticles are the type nanotechnology is a capable approach in the development of drug delivery systems especially for those potent drugs whose clinical development failed due to their poor solubility, low permeability, inadequate bioavailability, and other poor biopharmaceutical properties. The present review provides a information about the polymeric nanoparticles [5].

10. CONCLUSION

The objective of this review is obtained the information about the technology used for preparing the polymeric nanoparticles for enhance the bioavailability of the poorly water soluble drugs and gives the knowledge about the use of ingredients such as polymer, co-surfactant, surfactant, solvent used for the preparation. In this review various researcher are focus on the evaluation of the polymeric nanoparticles because it's very important for formation of polymer based nanoparticles. Various difficulties are come for study the Nano size of the particles. Various method used for characterization of the polymeric nanoparticles Such as Morphology, Particle size distribution, Zeta potential, In vitro release of Polymer based nanoparticles. In this review we concluded that polymer based nanoparticles are useful for enhance bioavailability of BCS class-Ⅱ drugs. We were also prepared polymer based nanoparticles of Artemether for enhanced bioavailability.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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