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An Overall Review On Biopolymeric Nanoparticles Method of Preparation and their Applications

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***Abstract*: Biopolymers are referred to as materials that are either biodegradable, derived from renewable and non-renewable resources, or materials that are non-biodegradable and derived from renewable sources. Polymeric nanoparticles collide particles ranging in size from 10 to 1000nm. Drugs may be dissolved, entrapped, encapsulated, or attached to a nanoparticle matrix. Because these systems have very high surface areas, drugs may also be adsorbed on their surface. The many biopol5 (proteins and Polysaccharides) that have recently transformed the field of biocompatible and degradable natural biological materials are highlighted in this review on nanoparticles. The review is mainly focused on the types, methods of preparation, and application of biopolymeric nanoparticles.**

***Keywords*: Polymeric nanoparticles, biodegradable, nanoparticle matrix, biocompatible, renewable, non-renewable.**

1. Introduction

Nanotechnology is the study and controlled manipulation of materials at atomic, molecular, and macromolecular sizes. structures and devices with length scales ranging from tens to hundreds often soften [1] 1–100nm the term "nanotechnology" was presumably coined first Taniguchi in Japan [2], is an industrial branch where diameters on the scale of a Nanometer matter the importance of size and scale was stressed by several researchers. Highlighted nanoparticles' benefits over microspheres (>1metre) [3]. As an alternative to liposomes in drug delivery systems. To overcome the problem, technology is being used related to the stability of these vesicles in biological fluids and during storage (4) nanoparticles have grown up ubiquitous in science as well as in a wide range of daily consumer goods. Catalysts make use of synthetic inorganic nanoparticles. From metals or alloys to semiconductors, oxides, and sunscreens, and are manufactured from a wide range of materials. or other types of ceramics [5] Polymeric nanoparticles, in contrast to these materials, are synthesized for a variety of purposes. Polymers based on vinyl monomers, such as polystyrene and poly alkyl (meth) acrylates, are commonly used. There are only a few polyesters and polyurethanes used. Most of them are synthetic in origin the particles gain functionality as a result of this. Surface alteration via chemical means. Aside from the general subject of sustainability. [6] Nanoparticle technology has been increasingly important in recent years for boosting medicinal efficacy. The nano-particles are compatible with colloidal drug delivery systems. Technologies that provide drug targeting benefits through changed [7] as well as the improvement of body distribution cellular uptake [8], which is aided by the decrease of unwanted substances free medications, have hazardous adverse effects [9]. They also show electrostatic attraction, hydrophobic interactions, and covalent bonding as a drug loading processes. Furthermore, the presence of functional groups in protein-based nano-particles allows for a variety of surface modifications. groups on the surfaces of the nanoparticles, allowing for precise drug targeting to the location of the action. Polysaccharides are digested by the same enzyme that digests proteins [10]. In terms of Polysaccharides have advantages over synthetic polymers in terms of lengthening circulation time. This review details the latest developments in proteins and Polysaccharides. Based on a previous study, we hypothesized that biopolymeric nanoparticles are used to achieve a more favorable pharmacokinetic profile and greater therapeutic efficacy.

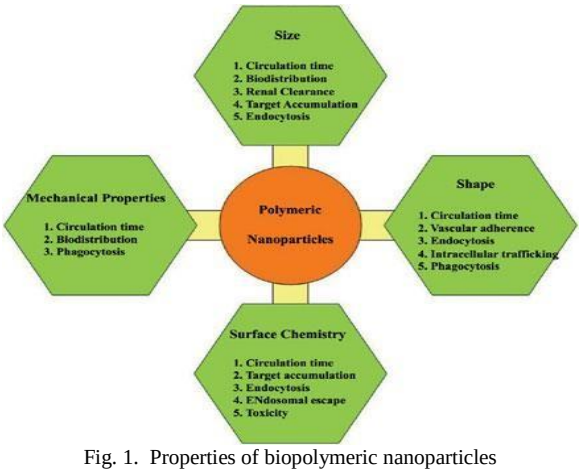

Fig. 1. Properties of biopolymeric nanoparticles

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2. Biopolymeric Nanoparticles

Albumin and non-biodegradable synthetic polymers like polyacrylamide and poly (methyl acrylate) were used to create the first biopolymer nanoparticles. [11-13].

Chronic toxicity from non-degradable polymer overloading in intracellular and/or tissue was quickly identified as a key barrier to systemic administration of polyacrylamide and poly (methyl acrylate) nanoparticles in humans. As a result, synthetic biodegradable polymers such as polyalkylcyanoacrylate, poly (lactic-co-glycolic acid), and polyanhydride [14–17] were used to create the sort of nanoparticles that gained a lot of interest. These biodegradable colloidal systems have been studied for their therapeutic potential in a variety of applications [18–23].

Despite the intriguing results published in the literature, these systems may also have toxicological issues [24, 25] Another restriction for bio nanoparticle-based delivery of hydrophilic molecules such as peptides, proteins, and nucleic acids (oligonucleotide and genes), which are known to have considerable therapeutic potential, is that they are hydrophilic molecules. This is because most of the polymers used to make these nanoparticles are hydrophobic, whereas proteins, peptides, and nucleic acids are hydrophilic. Make sit to encapsulate the medicine and protective from enzymatic breakdown [26]. As a result, more hydrophilic and naturally occurring materials have been studied for the creation of nanoparticles [27–29] Years ago, it was recognized that biodegradable nanoparticles (liposomes, virus-like particles (VLPs), proteins, and other biodegradable nanoparticles) might be used as effective drug delivery devices [30]. There as on for this is that in addition to the general benefits of nanoparticles, biopolymer nanoparticles, in particular, have several advantages, including the ease with which they can be made from well understood biodegradable polymers and their high stability in biological fluids and during storage [31].

Nanoparticles consisting of biodegradable polymers such as proteins and polysaccharides can be used as effective drug delivery vehicles for sustained, controlled, and targeted release, enhancing therapeutic effects while reducing adverse effects [32-34].

3. Types of Polymeric Nanoparticles

A. Protein/polypeptide nanoparticles

1. Protein-based nanoparticles
2. Silk–based nanoparticles
3. Collagen and Gelatin based nanoparticles
4. Beta–casein-based nanoparticles
5. Zein–based nanoparticles Protein
6. Albumin-based nanoparticles
7. Polypeptide nanoparticles

B. Polysaccharides nanoparticles

a) Alginate
b) Chitosan

1. Polysaccharide nanoparticles by crosslinking
2. Polysaccharide nano particles by Polyion–complex
3. Polysaccharide nano particles by self–assembly

4. Characterisation of Nanoparticles

A. The efficiency of Entrapment (%)

The amount of drug trapped in nanoparticles was calculated as a percentage of the total drug added during nanoparticle manufacturing to determine the percentage of drug entrapment. Using a 0.1 syringe filter, the free drug was measured.

% Entrapment Efficiency= (unfiltered–filtered/unfiltered) *100

B. Composition of Drugs

With minor changes, the drug content of MTX in MTXCHNP was determined using the HPLC technique [35]. In a nutshell, MTXCHNP was sonicated after a known amount of perchloric acid was introduced. This was then diluted with the mobile phase, filtered with a 0.22 m capsule filter, and run on HPLC with a mobile phase of methanol and PBS (pH6.0) (40:60) using an Acclaim 120 (C18, 3 m, 4.6*150 mm) column at 0.75 ml/min. MTX had an absorption of 306 nm.

The drug content and release kinetics of DEXCHNP were determined using an in-house validated approach that included the use of a Cary 60 UV–vis spectrophotometer (Agilent technologies). A known volume of sulphuric acid was mixed with 1 ml of produced nanoparticles, and the volume was increased to 3ml using distilled water. DEX's absorbance was measureddirectlyat270 nm and compared to the standard curve.

C. Zeta Potential and Size

Malvern Zeta sizer Nano ZS, which works on the concept of Dynamic Light Scattering, was used to estimate the size and polydispersity index (PDI) of CHNP (DLS). 1 ml of the nanoparticle-containing sample was deposited in a clear disposable cuvette and the measurement was performed using the Zeta sizer automated program. The particle size-distribution narrowness index (PDI) indicates how narrow the particle size distribution is [36]. A zeta sizer was also used to measure zeta potential (Malvern Zeta sizer Nano ZS).

D. Morphology of the Surface

Transmission Electron Microscopy (TEM) was used to analyze the morphology of CHNP in terms of size and form, with an FEI Tecnai G2 T30 (USA) voltage of 300 kV and there-commended magnification. On a carbon-coated copper grid, a thin coating of nanoparticles was placed. The grid was then dried in a desiccator before being put onto the microscope [37]. The scanning electron microscopeEVOLS10 (Carl Zeiss, Brighton, Germany) was used to complete the analysis. It functioned at a working accelerating voltage of 20.0 kV and has a high vacuum with amplification of 15000X. The lyophilized samples were spread on aluminum stubs with double-sided adhesive tape, then gold bombarded to charge the surface before being examined under a microscope. The image was processed using the Smart SEM software tool [38].

E. X-ray diffraction study

On a Bruker High-resolution X-ray diffractometer, powders-

ray diffraction (XRD)graphs for chitosan, MTX, MTXCHNP, DEX, and DEXCHNP were recorded throughoutthe20 a range of 5–80.

F. Study of Drug- Excipient Interactions

The Cary 630 FTIR was used to analyze the drug-excipient interaction (An Agilent technology. The sample was placed on the instrument's diamond ATR, and the Microlab PC program was used to observe the peaks.

5. Method of Preparation

Emulsification, desolvation, and coacervation are the three most prevalent processes for making protein and polysaccharide-based nanoparticles [39].

The synthesis of nanoparticles can be done in an environmentally responsible man materials have been used in the formation of nanoparticles in this method, and they can be used as a capping agent as well as a stabilizing agent [40,41]. The tiny particles are the biopolymer nanoparticles were chosen because of their small size, flexible manufacturing, and large surface area Drug delivery vehicles that are easy to use. Several biomaterials, such as collagen, could be used to make nanoparticles. Polysaccharides, proteins, and phospholipids [42-44]. Silk, keratin, collagen, elastin, maize, and other natural materials Soy protein has been used in a variety of nanoparticle investigations, including medication delivery and medicinal applications [45-48]. Drug delivery systems have has been utilized in medicine for illness prevention, diagnosis, and treatment. Before the discovery of microencapsulation, drug administration relied primarily on cataplasms or oral ingestion of herbal constituents, both of which are only partially successful while offering unnecessary health risks to the patients on whom they were employed [49-51]. They were recently supplemented by the electrospray drying process.

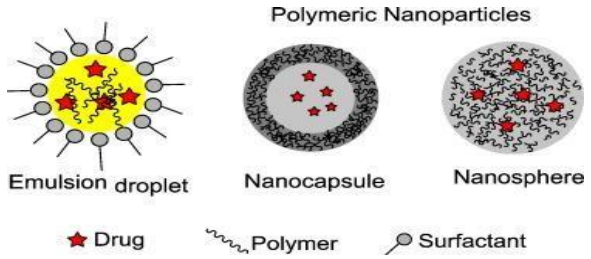

Fig. 2. Types of nanoparticles

6. Emulsification

The spontaneous emulsification that occurs when an organic phase and an aqueous phase are mixed (scheme 1(a)) provides the basis for nano-emulsion production. The phase of life that is organic is a homogenous mixture of oil, a lipophilic surfactant, and other ingredients. The aqueous phase consists of a water-miscible solvent, whereas the water-miscible solvent [52] of a hydrophilic surfactant and water This strategy is flexible. The dissolving of hydrophobic compounds in a liquid and organic solvent is emulsified with an aqueous medium. process solution with a high shear rate, as a result, every minute droplets(50–100nm) are formed. Evaporation removes the organic solvent after emulsification, leaving stable solid nanoparticle dispersions [53-55]. The most important need for organic solvent is the downside of this procedure and then taking it away. Furthermore, organic solvent residues may result in a harmful problem.

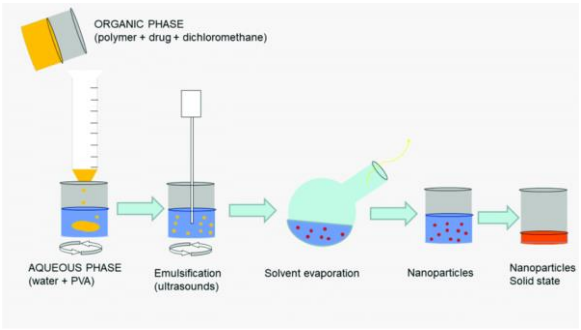

Fig. 3. Emulsification process

7. Desolvation

Marty et. al [56] employed a different strategy for nanoparticle manufacturing that entailed slowly adding a desolvation agent to the protein solution such as natural salts or alcohol. The tertiary structure of the molecule is altered by the desolvation component protein. Protein desolvation reaches a critical level when it reaches the critical level of desolvation. Co esteretal [57,58] developed a two-step desolvation technique for the production of gelatin nanoparticles which is a modification of the desolvation approach. In the low molecular gelatin fractions, the first desolvation process. De canting removes the contaminants in the supernatant while decanting removes the contaminants in the filtrate. Second, the silt contains high molecular fractions. At pH 2.5, the salts are redissolved and then resolved again. The Centrifugation can quickly purify the resultant particles. As well as redispersion.

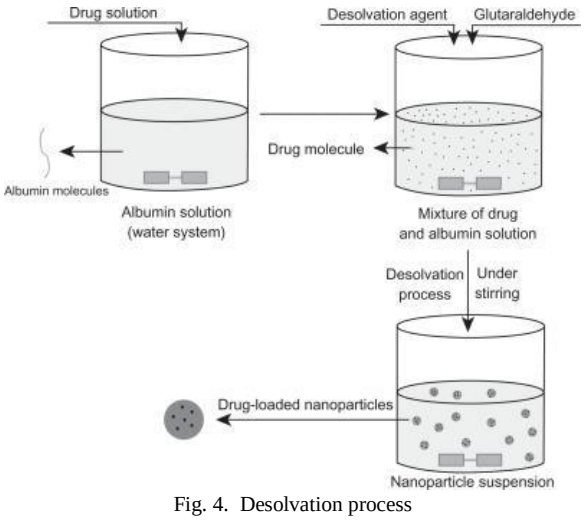

Fig. 4. Desolvation process

8. Coacervation

The coacervation method is similar to the desolvation method in that it uses an organic solvent such as acetone or ethanol to produce small coacervates from an aqueous protein

solution. The addition of crosslinking to coacervates limits them. a chemical, such as glutaraldehyde [59]. The distinction The varied concentrations, agitation, speed, the molar ratio of protein / organic solvent, and organic solvent addition rate of coacervation and desolvation methods characteristics that influence the fabrication process to achieve the intended result [60].

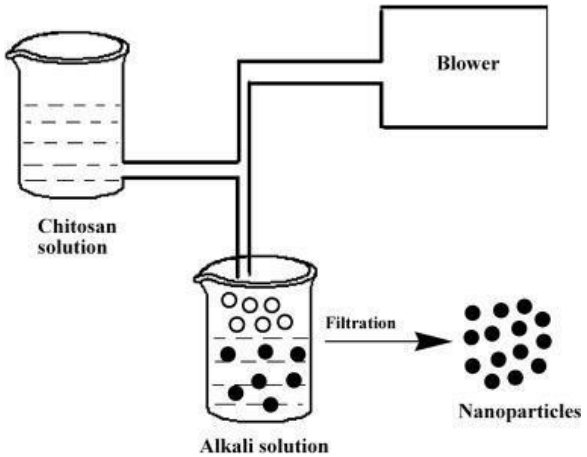

Fig. 5. Coacervation process

9. Electron Spray Drying

The electrospraying approach produces protein particles that are generally monodisperse and physiologically active. This procedure entails dissolving the dry powder into a protein solution. in a solution that can be electro sprayed. The solution dispersion Dry residues are collected after solvent evaporation. on appropriate deposition substrates Insulin nanoparticles of various size. This approach produced nanoparticles with diameters ranging from 88 to 110 nm [61]. The synthesis rate of nanoparticles increases as well their dimensions. The electro sprayer's biological activity method does not affect protein-based nanoparticles conditions.

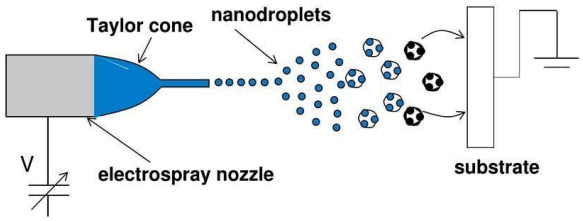

Fig. 6. Electron spraying process

10. Applications

Recently, multifunctional nanomaterials for cancer imaging and therapy have been developed [62,63]. For medication delivery, many functional nanomaterials have been tried as imaging agents and diagnostic sensors [64] Carbon nanotubes, gold nanoparticles for gene and medication delivery, magnetic nanoparticles, and silica nanoparticles have been explored [65-68]. Nanotechnology has recently received a lot of attention for its use in cancer treatment and prevention diagnosis. Nanoparticles can effectively treat tumors by transporting chemotherapeutic drugs to the tumor's location. Generation and progression [69,70] The theranostic protocol demonstrate a well-coordinated strategy for allowing the body to heal itself. Nanoparticles are used to diagnose and treat patients at the same time. Edible coatings containing integrated silver nanoparticles have already been tested on a variety of meals, including fruits and vegetables, meat, and cheese. Nonetheless, the research has so far been limited to a laboratory setting. As a remedy, using coating materials on fresh and minimally processed fruits and vegetables Multiple experiments have been conducted to reduce spoiling and increase shelf life during post-storage. In a study conducted by Sharanya et al. [71], it was discovered that apple and sapota storage periods differed. Covered tomato, chili, and aubergine were kept covered for 25 days, and covered tomato, chili, and aubergine were kept covered for 30 days. The duration of storage was increased to 21, 23, and 30 days, respectively. Moussa et al., in a separate study [72] Nanoparticle-based delivery technologies have the potential to improve pharmaceutical stability, prolong the therapeutic effect and enable enteral or parenteral administration. administration, which may aid in the prevention or reduction of pharmacological adverse effects. cellular outflow, degradation, and metabolism [73-76]. Protein nanoparticles (figure 1) can convey information. a variety of drugsthatcrosstheblood-brainbarrieronaregularbasisYouwillnotbeabletoovercomethis

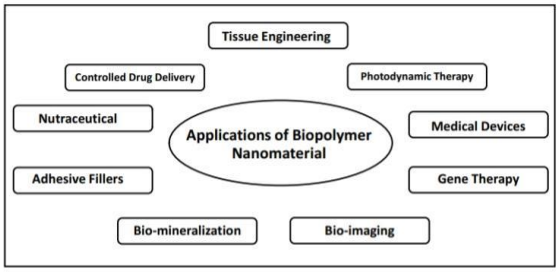

Fig. 7. Applications

Barrier after intravenous administration. A wide range of Several authors has demonstrated a high proclivity for Protein nanoparticles build up in some malignancies. For example,5-fluorouracilbindstoavariety of cytotoxic drugs. Paclitaxel and doxorubicin in albumin or gelatin nanoparticles. In the face of experimental challenges, the efficacy was considerably improved. Tumors or human malignancies were transplanted into nude mice. The hydrophilic nature of chitosan nanoparticles results in longer circulation in the blood, as reported by Allemann et al [77] for the hydrophilic nature of chitosan nanoparticles. nanoparticles. As a result, hydrophilic systems are capable of controlling not just the flow of water, but also the flow of the rate at which drugs are administered to extend the length of treatment not only the therapeutic effect but also the delivery of the medicine to specified locations. [78]. Chitosan nanoparticles with surface modifications are also used. Appropriate for the trapping and release of proteins in a regulated manner Ethylene oxide propylene oxide block, for example, ethylene oxide, propylene oxide issue in vaccinations [79]. The advantages of polymers made from renewable resources are currently most obvious in biomedical applications. One of the key advantages of such a

Biocompatibility and unique biochemical (enzymatic) or chemical (hydrolytic) breakdown is an important aspect of systems. importance when a system like this is proposed for use in organisms that are alive. Aside from the utilization of proteins particularly, For the most part, gelatinization is the formulation of nanoparticles. Particularly polysaccharides and polyesters are used in relevant systems identified in the literature (lactic acid). Apart from it, polystyrene beads, nanoparticles created from commercially available polystyrene beads The most often utilized polymeric materials are those made from poly (lactic acid) or its derivatives. Massive Biomedical nanoparticulate systems Only a portion of the massive This section can account for the number of publications. I'm hoping to offer the reader an idea of the possibilities and point in the right direction. Microencapsulation to in-depth biomedicine Adsorption, covalent bonding, and matrix are the other three basic ways for making bioartificial organs and artificial cells, respectively. entrapment. Cells have been encapsulated in microcapsules made of natural or synthetic polymers. Bioactive compounds (mammalian and microbial) (enzymes, proteins, and pharmaceuticals) [80]. The main advantages of this method are that cells or bioactive agents can be used. A microporous semipermeable membrane isolates them from the body and the encapsulated substance. As a result, it is safe from destruction. a matrix that is closed This type of device can be implanted and utilized as an artificial organ, a bioreactor, or to treat disease: In many circumstances, successful chemotherapy is restricted by the patient's ability to tolerate it. Non-targeted bodily areas are harmed by the drug's hazardous side effects nano capsulation polymers must be nontoxic and sterile, and they must not interact with the host Furthermore, the capsular materials' mechanical robustness is crucial, especially when long-term implantation is required. because the capsules must be able to survive the host's circulating fluids generate hydrodynamic forces. Furthermore, the capsule membrane must be intact. be permeable to nutrients and oxygen but not to water Immune cells and antigens [81]. Microencapsulation is most commonly done with polymer hydrogels [81,82]. Membranes with many components Polymers can be synthetic, semi-synthetic, or natural. The preparation of immune isolation barriers has shown significant potential. The most important encapsulation criteria and the systematic evaluation of nearly a thousand polymers. In recent papers [83-85], these issues have been discussed. Even though numerous polymers can be utilized to make capsules. Nevertheless, only a few have been used substantially. Covalent attachment of biotin-binding proteins to the surface of gelatin nanoparticles allows biotinylated drug targeting ligands to be bound by the avidin-biotin complex. One of the tactics explored was formation [86-88]. To release, thiolated gelatin nanoparticles were created. a heavily integrated nucleic acid molecule lowering the environmental impact [89]. These nanoparticles can due to their adaptability, can suit specific controlled release criteria in crosslinking and chemical modification This was reinforced by the fact that Kushibiki and Tabata [90] demonstrated this in 2005 using DNA that has been changed with poly (ethylene glycol) (PEGylated) nanoparticles of gelatin PEGylation of gelatin was also successful. In vivo, it is favorable to a long-circulating delivery method, as well as BT/20 human breast cancer cells [91]. for example, can be used to target tumor cells.] tenuous cells Chitosan has been used in the pharmaceutical industry for many years. Films, beads, and intragastric floating are just some of the options. Tablets, microspheres, and nanoparticles. [92-96] It was used as a delivery vehicle for drugs. [97-100].

11. Future Scope

Therearestillafewobstaclestoovercomeinthecreationofbiopolymer-based nanoparticles:

1. Protein and polysaccharide-based nano structure preparation procedures must be improved in order to obtain equally dispersed and stable nanoparticles.
2. The characteristics and applications of protein and polysaccharide-based nanoparticles formed action delivery and therapeutic purposes are still being researched.
3. These biopolymeric nanoparticles' cytotoxicity, biodegradability, biocompatibility, and immunological response must all be assessed before they can be used in clinical drug delivery.
4. Because the research and manufacturing of biopolymeric nanoparticles are still in the laboratory, biologists and chemical engineers will need to collaborate to produce the nanoparticles on a big scale.
5. By combining bioengineering, chemical modification, and nanomaterials sciences in the design of nanoparticulate structures, the drug delivery system's pharmacokinetics and biodistribution will be improved.

12. Conclusion

Theranostic nanoparticles are rapidly being developed for application in the treatment of diseases such as cancer and tuberculosis. Because of their tumor homing abilities and selectivity, biopolymer nanoparticles hold promise in cancer therapy and diagnosis. Biopolymers are natural macromolecules derived from animals and plants, making them readily available and renewable. Biopolymers are attractive targets for research and development in the field of theranostics because of their biodegradability and adjustable features. Nanoparticles manufactured from biopolymer-based materials can be easily processed and are often biocompatible. These biopolymers have a high surface-to-volume ratio which means they have a lot of room for macromolecule attachment. They provide for a regulated release of encapsulated pharmaceuticals with a long residence duration at drug absorption sites. The surface of nanoparticles can be easily manipulated to increase blood circulation times and render them immune. It's critical in the treatment of disorders like cancer, where the immune system is al is ready under strain. By coating the nanoparticles' surfaces with the active targeting ligand, the nanoparticles' tumor-targeting efficiency might be increased. The nanoparticles could be employed as a convenient integrated platform for developing safer and more successful drug

delivery systems for the treatment of lethal diseases that combine diagnosis, therapy, and monitoring activities. Noninvasivereal-time monitoring of drug efficacy and treatment success can assist clinicians in making timely decisions and optimizing drug doses and treatment plans. Because each theranostic modality has its own set of strengths and limitations, there are a few hurdles to overcome before theranostic nanoparticles may be used effectively in clinical settings. To achieve synergistic effects from nanoparticles, it is critical to choose the best combination of medicinal and diagnostic components. Theranostic biopolymer development based on nanoparticle system development should be thoroughly investigated for human and environmental safety. Nanoparticles with well-defined structures that can be synthesized repeatedly and are predominantly made of biodegradable and/or biocompatible building blocks can be considered great candidates for future research.

References

[1] Gao J H and XuB 2009 NanoToday 437
[2] TaniguchiN1983Ann. CIRF2 573
[3] Meclean S, Processer E, O'Malley D, Clark N, Ramtoola Z and Brayden D 1998 Eur. J.Pharm.Sci.6153.
[4] Oppenheim RC1981, Int. J. Pharm. 8217.
[5] Daniel and Astruc, 2004; Astrucetal.,2005; Kamat, 2007; Vallet-Regietal., 2007; Naetal., 2009; Beckeretal., 2010; Muñoz-Espíetal., 2012
[6] Musto,2013
[7] KreuterJ1983Pharm.ActaHelv.58217
[8] SchaferV, von Briesen H, Andreesen R, Steffan A M, Royer C, Troster S, Kreuter J and Rubsamen-Waigmann H1992 Pharm. Res. 9 541
[9] Narayani R and Rao K P 1993Int. J.Pharm.9585
[10] Mizrahy, S.; Peer, D. Polysaccharides as building blocks for nano therapeutics. Chem.Soc.Rev.2012,41,2623–2640
[11] ScheffelU,Rhodes B A,NatarajanTK andWagner H N 1972 J.Nucl.Med. 13498
[12] Birrenbach G and Speiser P, 1976, J.Pharm.Sci.651763
[13] KreuterJ andSpeiserPP 1976Infect.Immun.13204
[14] Couvreur P, Kante B, Rol and M, Guiot P, Bauduin P and Speiser P, 1979, J.Pharm. Pharmacol.31311
[15] Gurny R 1981 DrugDev. Ind.Pharm.71
[16] Vauthier-Holtzscherer C, Benabbou S, Spenlehauer G, Veillard M and Couvreur P, 1991, STP Pharm. Sci. 1 109
[17] Allemann E, Leroux J C, Gurny R and Doelker E, 1993, Pharm.Res.101732
[18] Mathiowitz E et al, 1997, Nature, 386410.
[19] Couvreur P and Vauthier C, 1991, J. Control. Release, 17187.
[20] Couvreur P and Vauthier C, 1994, Drug Absorption Enhancement Concepts, Limitations and Trends ed. AGde Boer (Leiden Amsterdam: Harwood Academic), p. 457.
[21] Couvreur P, Dubernet C and Puisieux F, 1995, Eur. J. Pharm. Biopharm. 412.
[22] Fattal E, Vauthier C, Aynie I, Nakada Y, Lambert G, Malvy C and Couvreur P, 1998, J. Control. Release, 53137.
[23] Labhasetwar V, Song C and Levy R J 1997, Adv. Drug Deliv. Rev. 2463.
[24] Maassen S, Fattal E, Müller R H and Couvreur P, 1993, STP, Pharma. 311
[25] Fernandez-Urrusuno R, Fattal E, Porquet D, Feger J and Couvreur P, 1995, Toxicol. Appl. Pharmacol., 130272.
[26] Emile C, Bazile D, Herman F, Helene C and Veillard M, 1996, Drug Deliv., 3187.
[27] Rajaonarivony M, Vauthier C, Couarraze G, Puisieux F and Couvreur P, 1993, J. Pharm. Sci., 82912.
[28] Wang N and Wu X S, 1997, Pharm. Dev. Technol., 2135.
[29] Calvo P, Remunan-Lopez C, Vila Jato J. L and Alonso M. J, 1997, Pharm. Res., 141431.
[30] Kumaresh S. S, Tejraj M. A, Anandrao R. K and Walter E. R, 2001, J. Control. Release, 70. 1.
[31] Mua L and Seowc P H, 2006, Colloids Surf., B, 4790.
[32] CouvreurP,GrefR,AndrieuxKandMalvyC2006Prog.SolidStateChem.342 31
[33] KreuterJ1978Pharm.ActaHelv.5333
[34] MartyJ J,OppenheimerRC andSpeiserP 1978Pharm
[35] Jia M, Li Y, Yang X, Huang Y, Wu H, Huang Y, et al. Development of both methotrexate and mitomycin C loaded PEGylated chitosan nanoparticles for targeted drug delivery and synergistic anticancer effect. ACS Appl Mater Interfaces. 2014;6:11413–23.
[36] Verma AK, Sachin K, Saxena A, Bohidar HB. Release kinetics from bio-polymeric nanoparticles encapsulating protein synthesis inhibitor-cycloheximide, for possible therapeutic applications. Curr Pharm Biotechnol [Internet]. 2005;6:121–30.
[37] Verma AK, Chanchal A, Chutani K. Augmentation of antitumor activity of cisplatin by pectin nanoconjugates in B–16 mouse model: pharmacokinetics and in–vivo biodistribution of radiolabeled, hydrophilic nanoconjugates.IntJNanotechnol.2012;9:872–86.
[38] Tariq M, Alam MA, Singh AT, Panda AK, Talegaonkar S. Surface decorated nanoparticles as surrogate carriers for improved transport and absorption of epirubicin across the gastrointestinal tract: Pharmacokinetic and pharmacodynamic investigations.Int. J. Pharm.
[39] LangerK,BalthasarS,VogelV,DinauerN,VonBriesenHandSchubertD2003 Int.J. Pharm. 257 169
[40] Nune, S. K., Chanda, N., Shukla, R., Katti, K., Kulkarni, R. R., Thilakavathy, S., Mekapothula, S., Kannan, R.&Katti, K.V.Greennanotechnologyfromtea:phytochemicalsinteaasbuildingblocks forproductionofbiocompatiblegoldnanoparticles.J. material scheme., 2009, 19(19), 2912-2920.
[41] Terracciano, M., De Stefano, L. & Rea, I. Diatoms Green Nanotechnology forBiosilica-BasedDrugDeliverySystems. Pharmaceutics,2018, 10(4),242.
[42] Dufresne,A.Polysaccharidenanocrystalreinforcednanocomposites.Canad. J.Chem.,2008, 86(6),484-494.
[43] Kwok,P.C.L.,Tunsirikongkon,A.,Glover,W.&Chan,H.-K.Formationofproteinnano-matrixparticleswithcontrolledsurfacearchitectureforrespiratorydrugdelivery.Pharmaceuticalresearch,2011, 28(4), 788-796.
[44] Aisha, A. F. A., Majid, A. M. S. A. & Ismail, Z. Preparation and characterization of nanoliposomes of Orthosiphonstamine use the ethanolic extract in soybean phospholipids. BMCbiotechnology, 2014, 14(1),23.
[45] Bessa, P. C., Machado, R., Nrnberger, S., Dopler, D., Banerjee, A., Cunha, A. M., Rodrguez-Cabello, J. C., Redl, H., van Griensven, M. & Reis, R. L. Thermoresponsiveself-as. J. controlled release,2010, 142(3), 312-318.sembled elastin-based nanoparticles for delivery of BMPs
[46] Dickerson,M.B.,Sierra,A.A.,Bedford,N.M.,Lyon,W.J.,Gruner,W.E.,Mirau,P.A.&Naik,R.R.Keratin-basedantimicrobialtextiles,films,andnanofibers.JournalofMaterials Chemistry B, 2013,1(40), 5505-5514.
[47] Numata, K. & Kaplan, D. L. Silk-based delivery systems of bioactive molecules.Advanceddrugdelivery reviews, 2010, 62(15), 1497-1508.
[48] Paliwal,R.&Palakurthi,S.Zeinincontrolleddrugdeliveryandtissueengineering.J.controlledrelease,2014,189,108-122.
[49] Noda, K., Saita, M., Hirano, M., Ikeura, Y., Taniguchi, Y., Hashiguchi, T., Kose, Y.,Takada,Y.,Kyoya,E.&Nakagawa, A.Ketorolac-containingfomentations,1996.
[50] Shimamura, T., Tairabune, T., Kogo, T., Ueda, H., Numajiri, S., Kobayashi, D. &Morimoto, Y. Investigation of the latest method for the topical application of pharmaceutical preparations: Release test of cataplasm including nonsteroidal anti-inflammatory drugs using artificial sweat. Chem.Pharmaceutical Bulletin, 2004, 52(2),167-171.
[51] Yamaguchi,T.&Kuribayashi,M.Drugcontainingpatch,GooglePatents,2010.
[52] BouchemalK,BriançonS,PerrierEandFessiH 2004Int.J.Pharm.280241
[53] SjöströmB,Kaplun A,TalmonYandCabaneB1995Pharm.Res. 1239
[54] Gao Z, ShuklaAJ, JohnsonJRand Crowley WR 1995Pharm.Res. 12 857
[55] JahanshahiMandBabaeiZ2008 Afr.J. Biotechnol.7 4926
[56] MartyJ J,OppenheimerRCandSpeiserP 1978Pharm.ActaHelv.5317
[57] CoesterC,NayyarP andSamuelJ 2006Eur.J.PharmBiopharm.62306
[58] CoesterCJ,LangerK,VonBriesenHandKreuterJ 2000J.Microencapsul.17187
[59] LinW,Coombes A,Davies M,Davis S andIllumL1993J.DrugTarget.1237
[60] JahanshahiM,NajafpourGandRahimnejadM 2008Afr.J.Biotechnol.7362
[61] GomezA,BinghamD,DeJuanLandTangK1999Mater.Res.Soc.Symp.Proc. 550 101

[62] Liong, M., Lu, J., Kovochich, M., Xia, T., Ruehm, S. G., Nel, A. E., Tamanoi, F. &Zink,J.I. Multifunctional inorganic nanoparticles for imaging, targeting, and drug delivery.ACS Nano, 2008,2(5), 889-896.
[63] Murphy,C.J.,Gole,A.M.,Stone,J.W.,Sisco,P.N.,Alkilany,A.M.,Goldsmit, E.C.&Baxter,S.C.Goldnanoparticlesinbiology:beyondtoxicitytocellulari maging.Accounts of chemicalresearch,2008, 41(12), 1721-1730.
[64] McFarland, A. D. & Van Duyne, R. P. Single silver nanoparticles as real-time optical sensors with zeptomole sensitivity. Nano Letters, 2003, 3(8), 1057-1062.
[65] Soppimath,K.S.,Aminabhavi,T.M.,Kulkarni,A.R.&Rudzinski,W.E.Biod egradable polymericnanoparticlesasdrugdeliverydevices.J.controlledrelease,2001, 70(1-2), 1-20.
[66] Bharali, D. J., Klejbor, I., Stachowiak, E. K., Dutta, P., Roy, I., Kaur, N., Bergey, E.J., Prasad, P. N. &Stachowiak, M. K. (2005). Organically modified silica nanoparticles: a nonviral vector for in vivo gene delivery and expression in the brain. P.N.A.S., 102(32),11539-11544.
[67] Slowing, I. I., Vivero-Escoto, J. L., Wu, C.-W. & Lin, V. S. Y. Mesoporous silica nanoparticles as controlled release drug delivery and gene transfection carriers. Advanceddrugdelivery reviews, 2008,60(11), 1278-1288.
[68] Mitragotri, S., Lammers, T., Bae, Y.H., Schwendeman, S., DeSmedt, S.C., Leroux, J. C., Peer, D., Kwon, I. C., Harashima, H. & Kikuchi, A. Drug delivery research for the future expanding the nano horizons and beyond, JControlRelease.2017,28;246:183-184.
[69] Knopov, V., Witte, R. P., Karmali, P., Lee, R., Webb, D. & Akopian, V. Method of producing lipid nanoparticles for drug delivery, GooglePatents,2008.
[70] Sahoo, S. K., Misra, R. & Parveen, S. Nanoparticles: a boon to drug delivery, therapeutics, diagnostics, and imaging. In Nanomedicine in cancer, Pan Stanford, 2017, pp. 73-124.
[71] Sharanya Devadiga, B.; Shetty, D.; Lakshmi, G.M.S.; Packiyam, J.E.; Bhat, R.P. Synthesis of Chitosan Silvernanoparticles from Chitin of Crustacean shells and Its Applications. Int. J. Curr. Res. Chem. Pharm. Sci. 2016,3, 1–5.
[72] Moussa, S.H.; Tayel, A.A.; Alsohim, A.S.; Abdallah, R.R. Botryticidal activity of nanosized silver-chitosan composite and its application for the control of gray mold in strawberry. J. Food Sci. 2013, 78, M1589–M1594.
[73] Sarmento B, Ribeiro A, Veiga F, Sampaio P, Neufeld R andFerreira D 2007 Pharm. Res. 24 2198
[74] Pan Y, Li Y J, Zhao H Y, Zheng J M, Xu H, Wei G, Hao J Sand Cui F D 2002 Int. J. Pharm. 249 139
[75] De S and Robinson D 2003 J. Control. Release 89 101
[76] Florence A . 14 1997 Pharm.Res 259
[77] Allemann E, Leroux J C, Gurny R and Doelker E 1993Pharm. Res. 10 1732
[78] Wu Y, Yang W, Wang C, Hu J and Fu S 2005 Int. J. Pharm.295 235
[79] Calvo P, Remunan-Lopez C, Vila-Jato J L and Aloso M J1997 J. Appl. Polym. Sci. 63 125
[80] 8 Goosen, M. F. A., ed. (1993) Fundamentals of Animal Cell Encapsu-lation and Immobilization, CRC Press, Boca Raton, FL, USA
[81] 31 Jen, A. C., Wake, M. C. and Mikos, A. G. (1996) Biotechnol.Bioeng. 50, 357–364
[82] Wang, T. et al. (1997) Nat. Biotechnol. 15, 358–362
[83] Prokop, A., Hunkeler, D., DiMari, S., Haralson, M. A. and Wang, T. G. (1998) Adv. Polym. Sci. 136, 1–51
[84] Hunkeler, D., Prokop, A., Poweres, A., Haralson, M., DiMari, S.and Wang, T. (1997), Polym. News 22, 232–240
[85] Hunkeler, D. (1997) Trends Polym. Sci. 5, 286–293
[86] Wartlick H, Michaelis K, Balthasar S, Strebhardt K, Kreuter Jand Langer K 2004 j.Drug Target. 12 461
[87] Langer K, Coester C, Weber C, von Briesen H and Kreuter J2000 Eur. J. Pharm. Biopharm. 49 303
[88] Coester C, Kreuter J, von Briesen H and Langer K 2000 Int.J. Pharm. 196 147
[89] Kommareddy S and Amiji M 2005 Bioconjug. Chem.16 1423
[90] Kushibiki T and Tabata Y 2005 J. Biomater. Sci. Polym. 161447
[91] Kaul G and Amiji M 2002 Pharm. Res. 197 1061
[92] Berthold A, Cremer K and Kreuter J 1996 J. Control. Release, 39 17
[93] Calvo P, Remunan-Lopez C, Vila-Jato J L and Aloso M J1997 J. Appl. Polym. Sci. 63 125
[94] Felt O, Buri P and Gurny R 1998 Drug Dev, Ind. Pharm. 24979
[95] Giunchedi P, Genta I, Conti B, Muzzarelli R A A and ConteU 1998 Biomaterials 19 157
[96] Illum L 1998 Pharm. Res. 15 1326
[97] Hou W M, Miyazaki S, Takada M and Komai T 1985 Chem. Pharm. Bull. 33 3986
[98] Kawashima Y, Handa T, Kasai A, Kasai A, Takenaka H,Lin S Y and Ando Y 1985 J. Pharm. Sci. 74 264
[99] Miyazaki S, Yamaguchi H, Yokouchi C, Takada M, and Hou W M 1988 Chem. Pharm. Bull. 36 4033
[100] Shiraishi S, Imai T and Otagiri M 1993 J. Control. Releasen 25 217.