STM JOURNALS

International Journal of
Photochemistry and
Photochemical Research

Volume 3, Issue 1, 2025
January–June
DOI Journal: 10.37591/IJPPR

https://journals.stmjournals.com/ijppr

Review IJPPR

Biopolymer-based Nanoparticles: Advances in Fabrication, Characterization, and Biomedical Applications

Adebayo Samuel[1,*]

Abstract

*The emergence of biopolymer-based nanoparticles, particularly those composed of proteins and polysaccharides, has significantly transformed the landscape of biocompatible and biodegradable materials. These nanoparticles offer immense potential due to their ability to facilitate encapsulation and targeted delivery of bioactive compounds, enhancing therapeutic efficacy while minimizing side effects. This review explores the various fabrication techniques, including emulsification, desolvation, coacervation, and electrospray drying, emphasizing their advantages and limitations. The characterization of nanoparticles based on critical parameters such as size, surface charge, morphology, stability, and controlled release properties is discussed in detail, along with advanced analytical techniques for measurement. Furthermore, this article delves into the diverse biomedical applications of these nanoparticles, including drug delivery, wound healing, tissue engineering, and vaccine development. The review also highlights current challenges and future perspectives, focusing on scalability, regulatory considerations, and novel formulations that integrate multiple functionalities for enhanced performance. With ongoing advancements in nanotechnology and material science, biopolymer-based nanoparticles continue to be a promising avenue for various biomedical applications, fostering innovation in targeted therapies and regenerative medicine.***

Keywords: Biopolymers, nanoparticles, encapsulation, controlled release, biomedical applications

INTRODUCTION

Nanotechnology is a field that focuses on the manipulation and study of materials at the atomic, molecular, and macromolecular levels, with dimensions ranging from 1 to 100 nm. First introduced by Taniguchi, this discipline has gained immense significance due to its impact on material science and drug delivery systems. These nanoparticles have been developed as an alternative to liposomes, addressing stability issues in biological environments. The ability of nanoparticles to enhance drug efficacy, target-specific distribution, and cellular uptake makes them a valuable asset in pharmaceutical sciences. The selection of materials is based on multiple factors such as nanoparticle morphology, surface charge, permeability, biocompatibility, and drug release kinetics. This review highlights the advancements in biopolymer-based nanoparticles, with a focus on their fabrication methods, characterization techniques, and biomedical applications.

***Author for Correspondence**
Adebayo Samuel
E-mail: adebayosam60@gmail.com

[1]Assistant Professor, Department of chemistry, University of Nigeria, Nsukka (UNN)

Received Date: February 10, 2025
Accepted Date: February 14, 2025
Published Date: February 15, 2025

Citation: Adebayo Samuel. Biopolymer-Based Nanoparticles: Advances in Fabrication, Characterization, and Biomedical Applications. International Journal of Photochemistry and Photochemical Research, Volume 3, Issue 1. 2025; 3(1): 38–46p.

BIOPOLYMER NANOPARTICLES

The initial attempts at designing nanoparticles involved albumin-based formulations and synthetic non-biodegradable polymers such as

polyacrylamide and poly(methylacrylate). However, concerns regarding chronic toxicity due to intracellular accumulation led to a shift towards biodegradable synthetic polymers like polyalkylcyanoacrylate, poly(lactic-co-glycolic acid), and polyanhydrides. Although these materials showed promise, certain toxicity concerns persisted. Another challenge was the encapsulation of hydrophilic biomolecules, including peptides, proteins, and nucleic acids, due to the hydrophobic nature of synthetic polymers. Consequently, research expanded towards utilizing naturally occurring biopolymers to enhance biocompatibility and improve encapsulation efficiency.

Biodegradable nanoparticles, such as those based on proteins and polysaccharides, offer advantages such as ease of synthesis, stability in biological environments, and controlled drug release. These properties make them ideal candidates for targeted drug delivery and therapeutic applications [1-3].

PROTEIN-BASED NANOPARTICLES

Albumin-Based Nanoparticles

Albumin, a major plasma protein, is widely recognized for its biocompatibility, biodegradability, and non-immunogenic properties. Additionally, albumin functions as an extracellular antioxidant, providing protection against oxidative stress and toxic agents. These attributes have facilitated its application in drug therapy, particularly in tumor-targeting strategies and receptor-mediated drug delivery.

Albumin-based nanoparticles have also been explored for drug delivery across the blood-brain barrier, enabling central nervous system-targeted therapies.

Collagen-Based Nanoparticles

Collagen, a primary structural protein in vertebrates, is widely used in biomaterials due to its excellent biocompatibility and biodegradability. Its unique triple-helix structure and modifiable surface properties make it an attractive candidate for nanoparticle synthesis. Collagen nanoparticles can be enhanced with additional biomolecules like elastin, fibronectin, and glycosaminoglycans to improve their physicochemical and biological properties. Crosslinking agents such as glutaraldehyde and gamma radiation can further regulate biodegradability and drug release kinetics. These nanoparticles demonstrate high thermal stability, sterilization feasibility, and efficient cellular uptake, making them valuable for drug delivery applications.

Gelatin-Based Nanoparticles

Gelatin, derived from the partial hydrolysis of collagen, exists in two primary forms: Type A (acid-treated, pI 7.0–9.0) and Type B (alkaline-treated, pI 4.8–5.0). Gelatin nanoparticles offer advantages such as biocompatibility, biodegradability, and low immunogenicity, making them suitable for drug delivery applications. Their functional groups allow for chemical modifications, crosslinking, and derivatization, facilitating drug encapsulation and sustained release. Over the past three decades, gelatin nanoparticles have been widely explored for pharmaceutical applications due to their ease of synthesis and desirable physicochemical properties [4].

Silk Proteins—Sericin and Fibroin Nanoparticles

Silk fibers primarily consist of two main proteins: fibroin, a structural core protein, and sericin, a sticky, glue-like coating protein.

Fibroin

Fibroin is a hydrophobic glycoprotein that constitutes over 70% of the silk cocoon. Composed primarily of glycine, alanine, and serine (-Gly-Ala-Gly-Ala-Gly-Ser-), fibroin adopts an antiparallel β-pleated sheet structure, contributing to its semi-crystalline nature. This composition results in two phases: a highly crystalline β-sheet phase and an amorphous phase. It can be processed into various formats, including gels, membranes, scaffolds, hydrogels, and nanoparticles, offering advantages such as high porosity, biodegradability, and compatibility with cellular systems. The historical use of silk as

a suture material underscores its minimal foreign body response, further supporting its application in biomaterials and drug delivery systems.

Sericin

Sericin, a hydrophilic glycoprotein, constitutes 20–30% of the silk cocoon and functions as a binding agent. This water-soluble protein consists of polypeptides ranging in molecular weight from 24 to 400 kDa, with a high serine (40%) and glycine (16%) content. Structurally, sericin comprises approximately 35% β-sheet and 63% random coil, exhibiting a partially unfolded conformation. Apart from general nanoparticle advantages, sericin possesses intrinsic properties such as antioxidant and antitumor activity, enhancement of bioavailability of elements like Zn, Mg, Fe, and Ca, and anticoagulant effects when sulfated. Additionally, it promotes fibroblast proliferation, supports collagen synthesis, and accelerates wound healing without inducing inflammation, making it highly valuable in therapeutic applications.

Keratin

Keratin is a structural protein rich in cysteine, providing high mechanical strength through numerous disulfide bonds. It has recently been utilized in nanosuspensions, forming ultra-thin, transparent coatings suitable for cell proliferation studies. This innovation offers an alternative to conventional materials like collagen and fibronectin and presents potential applications in tissue engineering and regenerative medicine.

POLYSACCHARIDE NANOPARTICLES

Polysaccharide-derived nanoparticles play a crucial role in enhancing biocompatibility and optimizing drug delivery. These nanoparticles facilitate improved immobilization strategies and are being actively explored for novel pharmaceutical formulations.

Alginate

Its solubility is modulated by cationic interactions, with calcium ions inducing gelation. Alginate can also form polyelectrolyte complexes with polycations such as polyenimine, chitosan, and polylysine, further broadening its application in nanoparticle synthesis. Alginate-based nanoparticles enhance mucosal adhesion, prolong drug retention, and facilitate targeted delivery, making them valuable in therapeutic interventions.

Chitosan

Chitosan nanoparticles can be formed through polyelectrolyte complexation with DNA or through gelation in water-in-oil emulsions, allowing their use in gene therapy, vaccine delivery, and controlled drug release applications [5-7].

Here is the extracted table in text format:

FABRICATION TECHNIQUES

The synthesis of protein- and polysaccharide-based nanoparticles commonly employs methods such as emulsification, desolvation, coacervation, and electrospray drying.

Emulsification

Emulsification involves the spontaneous formation of nano-emulsions upon mixing an organic phase (comprising oil, lipophilic surfactant, and a water-miscible solvent) with an aqueous phase containing hydrophilic surfactants. Hydrophobic drugs are dissolved in an organic solvent and emulsified with an aqueous solution under high shear, yielding nano-sized droplets. Subsequent solvent evaporation results in stable nanoparticle dispersions. Despite its effectiveness, this method has limitations, including the requirement for organic solvents and the potential for residual toxicity Table 1.

Table 1. Milestones of silk protein nanoparticles, preparation and application in chronological order.

Protein	Method of Fabrication	Particle Size (nm)	Remarks
Silk fibroin	Precipitation using water miscible protic and polar aprotic organic solvents	35–125	Globular insoluble particles well dispersed and stable in aqueous solution
	Precipitation using water miscible protic and polar aprotic organic solvents	50–120	Matrix for immobilization of L-asparaginase
	Microemulsion	167	Color dye doped silk fibroin nanoparticles
	Conjugated covalently with insulin using crosslinking reagent glutaraldehyde	40–120	Insulin–silk fibroin nanoparticles bioconjugates
	Capillary microdot technique	<100	Sustained and long-term therapeutic delivery of curcumin to breast cancer cells
	Desolvation	150–170	Cellular uptake and control release studies
Silk sericin	Conjugation of sericin with activated PEG	200–400	Overcomes its problem of instability in water and insolubility in organic solvents
	Sericin–PEG self-assembled through hydrophobic interactions	204	Self-assembled nanostructures for immobilization and drug delivery
	Sericin–poly methacrylate core-shell nanoparticles by graft copolymerizing technique	100–150	Potential biomedical application as delivery systems
	Self-assembled silk sericin/poloxamer nanoparticles	100–110	Nanocarriers of hydrophobic and hydrophilic drugs for targeted delivery
	Self-assembled silk sericin nanostructures	–	Fractal self-assembly of silk protein sericin

Would you like any modifications or formatting improvements?

Here is the extracted table in text format:

Desolvation

Desolvation is another widely used technique, originally developed by Marty et al. This method involves the gradual addition of a desolvating agent (e.g., alcohol or salts) to a protein solution, altering its tertiary structure and inducing nanoparticle formation. Chemical crosslinking (e.g., with glutaraldehyde) stabilizes the nanoparticles. A refined version, developed by Coester et al., employs a two-step desolvation approach to enhance nanoparticle uniformity and stability. This method is particularly effective for gelatin nanoparticle synthesis and is widely adopted for drug delivery applications Table 2 [8-10].

Table 2. Milestones of alginate and its composite nanoparticles preparation and applications in chronological order.

Polymer	Method of Fabrication	Particle Size (nm)	Remarks
Alginate	Control of the gel formation of alginate by calcium ions	250–850	Evaluation for the drug-loading capacity with doxorubicin as a model drug
Alginate	Gelation in presence of calcium ions and further crosslinking with poly-L-lysine	–	Nanosponges are new antisense oligonucleotide carrier systems for specific delivery to lungs, liver, and spleen
Sodium alginate and BSA	Emulsion solidification method	166±34	Determination of the kinetic parameters of 5-FU sodium alginate-^{125}I BSA nanoparticles metabolism
Calcium alginate	Water-in-oil microemulsion followed by calcium crosslinking of glucuronic acid units	80	Examination of the nanoparticles for their potency as carriers for gene delivery
Alginate	Ionotropic pre-gelation of alginate	764–2209	Monitor the complexation of contrary

and chitosan	with calcium chloride followed by complexation between alginate and chitosan		charged polyelectrolytes as insulin nanoparticulate carriers
Alginate and chitosan	Induction of a pre-gel with calcium counter ions, followed by polyelectrolyte complex coating with chitosan	850±88	Development of an oral insulin delivery system having mild formulation conditions, high insulin entrapment efficiency for gastrointestinal release
Alginate and chitosan	Induction of a pre-gel with calcium counter ions, followed by polyelectrolyte complex coating with chitosan	750	*In vivo* evaluation of the pharmacological activity of the insulin-loaded nanoparticles
Alginate	Gelation in presence of calcium ions and further crosslinking with Eudragit E-100	200–950	*In vitro* release study revealed sustained release of gliclazide from gliclazide-loaded alginate nanoparticles
Alginate	Modified coacervation or ionotropic gelation method	205–572	Optimization of mucoadhesive nanoparticulate carrier systems for prolonged ocular delivery of the drug

Let me know if you need any modifications or formatting adjustments!

Coacervation

The coacervation method closely resembles the desolvation technique, involving the mixing of an aqueous protein solution with an organic solvent such as acetone or ethanol to generate tiny coacervates. The stabilization of these coacervates is achieved by introducing a crosslinking agent like glutaraldehyde. The primary distinction between coacervation and desolvation lies in the various parameters influencing the nanoparticle fabrication process.

Electrospray Drying

Electrospraying is an efficient technique for producing relatively monodisperse and biologically active protein nanoparticles. In this method, a protein solution is prepared by dissolving the dry protein powder in an electrosprayable solution. While a higher production rate results in increased particle size, the electrospraying process does not compromise the biological activity of protein-based nanoparticles.

CHARACTERIZATION OF NANOPARTICLES

Particle size, distribution, and charge significantly influence the physical stability and in vivo behavior of nanoparticles. Electron microscopy plays a crucial role in determining the overall shape of polymeric nanoparticles, which can have implications for their toxicity. Surface charge affects the stability, redispersibility, and in vivo performance of nanoparticles.

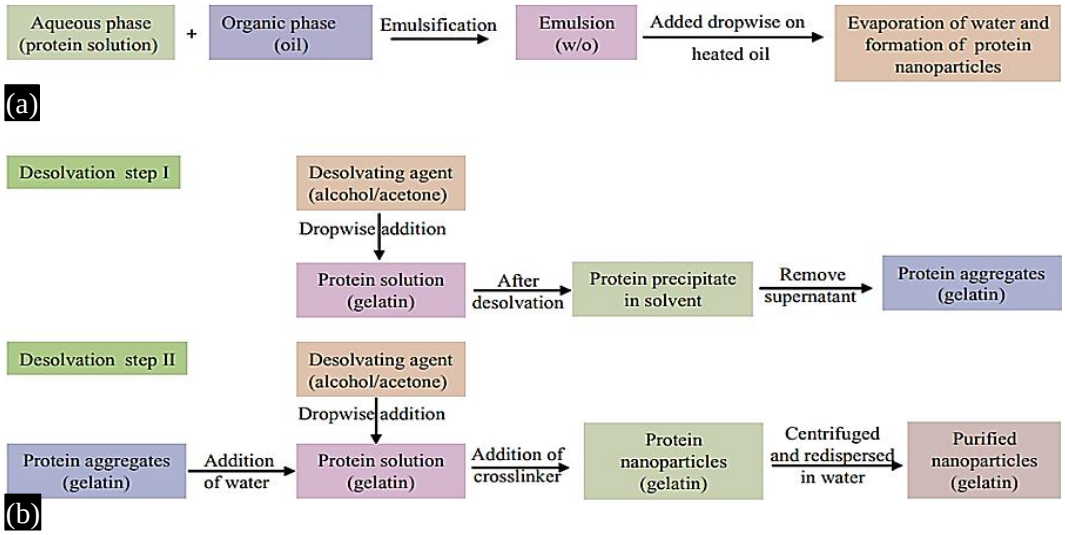

Figure 1. Schematic representation of nanoparticles preparation by (a) emulsification method [38, 119] and (b) two step desolvation method.

Particle Size

Nanoparticle size is a critical factor influencing drug release and targeting efficiency. Smaller nanoparticles provide a larger surface area, leading to faster drug release, whereas larger nanoparticles facilitate a more controlled and sustained release. However, smaller nanoparticles are more prone to aggregation during storage and transportation, necessitating a balance between size and stability. Figure Additionally, nanoparticle size plays a vital role in biosensor applications, as smaller particles improve enzyme immobilization efficiency by providing a larger surface area and minimizing diffusion resistance [11-15].

Dynamic Light Scattering (DLS)

This method involves the scattering of monochromatic laser light by nanoparticles in Brownian motion, where the Doppler shift caused by particle movement allows the determination of particle size. The technique is rapid, automated, and cost-effective, providing valuable data on size distribution and polydispersity index (PI).

Nanoparticle Tracking Analysis (NTA)

This technique employs an ultramicroscope to visualize the movement of particles under Brownian motion, followed by computational analysis to determine particle size using the Stokes-Einstein equation. NTA requires minimal sample preparation and offers rapid results.

Particle Morphology

Various microscopic techniques, including SEM, TEM, and AFM, are employed to assess nanoparticle morphology and surface roughness.

For SEM analysis, nanoparticle solutions must first be converted into dry powder, mounted on a sample holder, and coated with a conductive metal (e.g., gold). A focused electron beam scans the sample, and secondary electrons emitted from the surface provide information about its characteristics. However, nanoparticles must be vacuum-resistant, as exposure to the electron beam can damage polymeric materials [16].

Transmission Electron Microscopy (TEM)

TEM provides highly detailed morphological information by transmitting an electron beam through an ultrathin sample. Sample preparation for TEM is labor-intensive, requiring nanoparticles to be fixed using negative staining materials (e.g., phosphotungstic acid) or plastic embedding. An alternative method involves embedding samples in vitreous ice at liquid nitrogen temperatures to preserve their structure.

Atomic Force Microscopy (AFM)

AFM enables the imaging of nanoparticle surfaces at the atomic level without requiring conductive samples or extensive preparation. This technique scans the sample with a sharp probe and compiles the interactions into detailed surface images, making it particularly useful for biological and polymeric nanostructures.

Particle Stability

The colloidal stability of nanoparticles is assessed using zeta potential analysis, which measures the surface charge of nanoparticles. Laser Doppler anemometry evaluates particle velocity shifts, transforming electrophoretic mobility into zeta potential values. Most colloidal particles exhibit negative zeta potential values (-100 to -5 mV), which prevent nanoparticle aggregation through electrostatic repulsion, thereby enhancing stability.

Particle Structure

Understanding the structural modifications of proteins during nanoparticle synthesis is essential. Two key techniques used for this purpose are:

X-ray Diffraction (XRD)

XRD is a fundamental tool for analyzing the crystalline structure of nanoparticles, assessing phase composition, crystallite size, and lattice distortions. Samples are illuminated with X-rays (Copper Kα, 1.54 Å), and diffraction patterns are analyzed to determine structural characteristics.

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR provides insights into the structural details of proteins in solution by detecting the characteristic vibrations of molecular bonds.

Cellular Uptake and Cytotoxicity

Assessing nanoparticle cytotoxicity and cellular uptake is crucial for biomedical applications. Cytotoxicity is evaluated using MTT assays, which measure enzymatic reduction activity in viable cells.

Drug Loading and Release

The drug loading capacity of nanoparticles is determined using classical analytical techniques such as UV spectroscopy and high-performance liquid chromatography (HPLC). Encapsulation efficiency is assessed by [17] comparing the amount of encapsulated drug to the total drug used. Drug release studies monitor the controlled release of encapsulated bioactive molecules over time.

APPLICATIONS IN DRUG DELIVERY

Protein nanoparticles facilitate drug transport across the blood-brain barrier and accumulate in tumors, improving efficacy. Albumin and gelatin nanoparticles enhance the therapeutic performance of

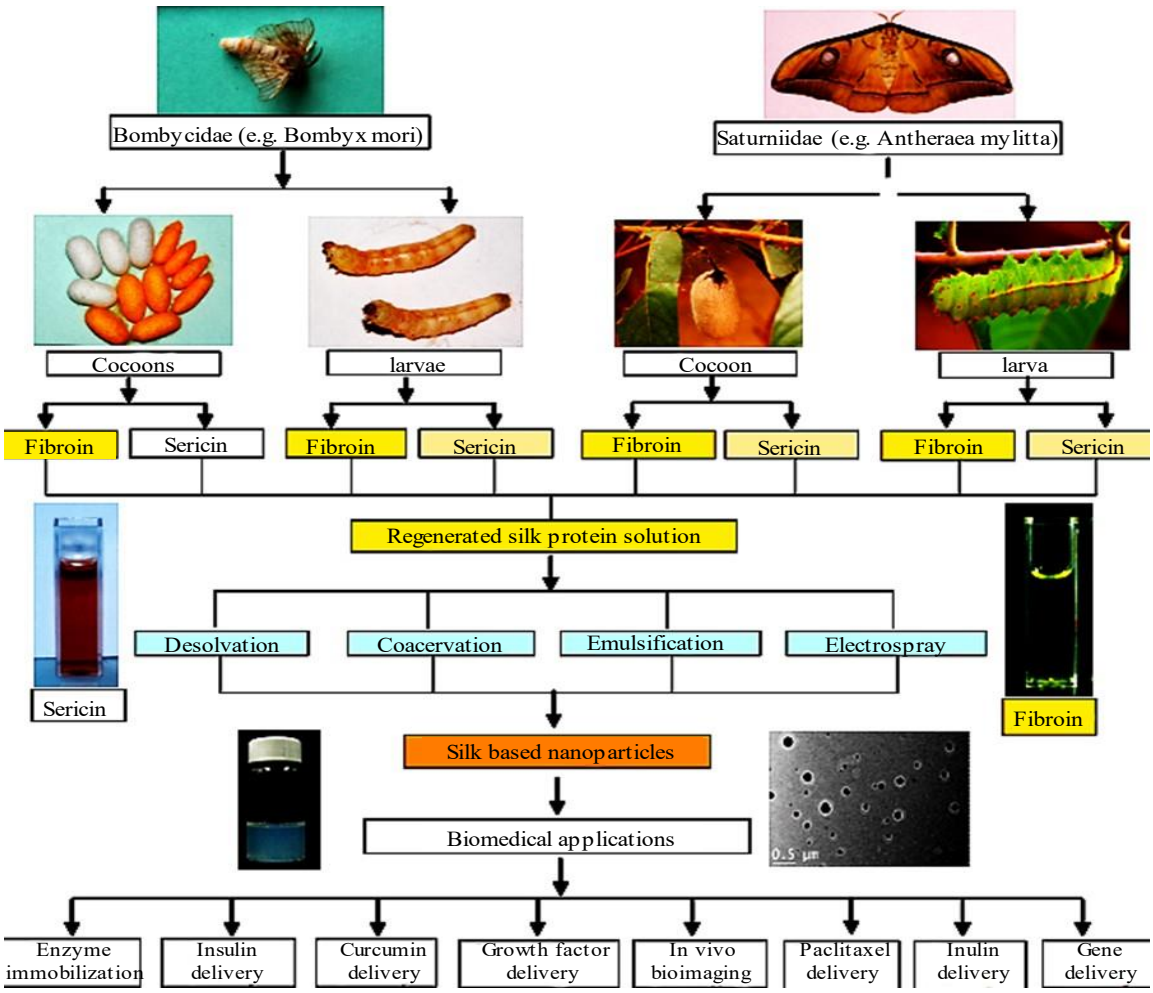

Figure 2. Extraction and utilization of silk proteins from different silk-producing organisms.

cytotoxic drugs such as 5-fluorouracil, paclitaxel, and doxorubicin. Additionally, gelatin nanoparticles improve bioavailability in ophthalmic drug delivery and serve as efficient gene delivery vehicles. Surface modifications, including PEGylation and thiolation, further optimize targeting and controlled drug release [18-20].

Figure 2. The isolated silk proteins are further processed and engineered to obtain the regenerated silk protein solution. The regenerated silk solutions are then further subjected to processes like desolvation, coacervation, emulsification and electrospraying to obtain the silk-based nanoparticles. These silk-based nanoparticles are further utilized in such biomedical applications as drug delivery, enzyme immobilization, growth factors delivery, in vivo bioimaging, gene delivery, etc.

CONCLUSION

1. Biopolymeric nanoparticles offer advantages such as biodegradability, biocompatibility, and non-toxicity.
2. Their fabrication involves emulsification, desolvation, coacervation, and electrospray drying methods.
3. Characterization techniques include DLS, SEM, TEM, AFM, XRD, and FTIR.
4. They have significant potential in drug and gene delivery applications.

Future Scope

1. Optimization of fabrication methods for stable, well-dispersed nanoparticles.
2. Further research on biopolymeric nanoparticles for clinical applications.
3. Evaluation of cytotoxicity and immune responses.
4. Large-scale production strategies.
5. Integration of bioengineering and nanotechnology to enhance drug delivery efficiency.

REFERENCES

1. Majumdar S and Basu S K 1991 *Antimicrob. Agents Chemother.* **35** 135
2. Nakagawa Y, Takayama K, Ueda H, Machida Y and Nagai T 1987 *Drug Des. Deliv.* **2** 99
3. Segura S, Espuelas S, Renedo M J and Irache J M 2005 *Drug Dev. Ind. Pharm.* **31** 271
4. Irache J M, Merodio M, Arnedo A, Camapanero M A, Mirshahi M and Espuelas S 2005 *Mini-Rev. Med. Chem.* **5** 293
5. Santhi K, Dhanaraj S A, Joseph V, Ponnusankar S and Suresh B 2002 *Drug Dev. Ind. Pharm.* **28** 1171
6. Kreuter J, Hekmatara T, Dreis S, Vogel T, Gelperina S and Langer K 2007 *J. Control. Release* **118** 54
7. Merodio M, Irache J M, Eclancher F, Mirshahi M and Villarroya H 2000 *J. Drug Target.* **8** 289
8. Lynn A K, Yannas I V and Bonfield W 2004 *J. Biomed. Mater. Res. B: Appl. Biomater. B* **71** 343
9. Barbani N, Giusti P, Lazzeri L, Polacco G and Pizzirani G 1995 *J. Biomater. Sci. Polym. Ed.* **7** 461
10. Lefebvre F, Gorecki S, Bareille R, Amedee J, Bordenave L and Rabaud M 1992 *Biomaterials* **13** 28
11. Ruderman R J, Wade C W R, Shepard W D and Leonard F 1973 *J. Biomed. Mater. Res.* **7** 263
12. Bender A, von Briesen H, Kreuter J, Duncan I B and Rubsamen-Waigmann H 1996 *Antimicrob. Agents Chemother.* **40** 1467
13. Schwick H G and Heide K 1969 *Bibl. Haematol.* **3** 111
14. Ward A G and Courts A 1977 *The Science and Technology of Gelatin* (New York: Academic)
15. Bajpai A K and Choubey J 2006 *J. Mater. Sci: Mater. Med.* **17** 345
16. Stevens K R, Einerson N J, Burmania J A and Kao W J 2002 *J. Biomater. Sci. Polym. Ed.* **13** 1353
17. Marios Y, Chakfe N, Deng X, Marios M, How T, King W and Guidoin R 1995 *Biomaterials* **16** 1131

18. DiSilvio L, Courtney-Harris R G and Downes S 1994 *J. Mater. Sci., Mater. Med.* **5** 819
19. Sinohara H, Asano Y and Fukui A 1971 *Biochem. Biophys. Acta* **237** 273
20. Asakura T and Kaplan D L 1994 *Encyclopedia of Agricultural Science* vol 4, ed C J Arntzen and E M Ritter (New York: Academic) p 1.

