Materials Horizons: From Nature to Nanomaterials

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Nabisab Mujawar Mubarak *Editors*

Nanotechnology for Biomedical Applications

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Materials Horizons: From Nature to Nanomaterials

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Contents

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Chapter 1
Introduction to Biomedical Applications in Nanotechnology

S. Archana, Devi Radhika, K. Yogesh Kumar, S. B. Benaka Prasad, and R. Deepak Kasai

1 Introduction

Nanomaterials have a unique advantage in medical applications because of their smaller structures and increased surface area [1–3]. Appropriate selection of substrate is essential to achieving the desired multifunctional properties that many applications need [4, 5]. One of the most common elements in the Earth's crust is carbon. In different forms, carbon atoms bond with each other to form various carbon allotropes, to produce a set of carbon-based Nanocomposites. These include nanodiamonds [6, 7] carbon dots [8, 9], carbon nanotubes [10, 11] graphene and its derivatives [12–14]. Metal nanocomposites are the types of materials that comprise metal or alloy as the substrate in which specific nanosized material is grafted. These composites include metal-ceramic characteristics, for example, ZnO, TiO_2, SiO_2, and CeO_2 [15, 16]. Polymer nanocomposites are generally used for their easy manufacturing, flexible and wear resistance properties. In contrast to ceramic materials, they have certain restrictions, such as limited strength and modulus [17, 18]. In a broad array of applications, nanomaterials are considered to be the efficient ones. This is a product of its remarkable electrical, optical, photocatalytic, and biochemical properties, large specific surface area, effective bandgap, including more significant biochemical activity.

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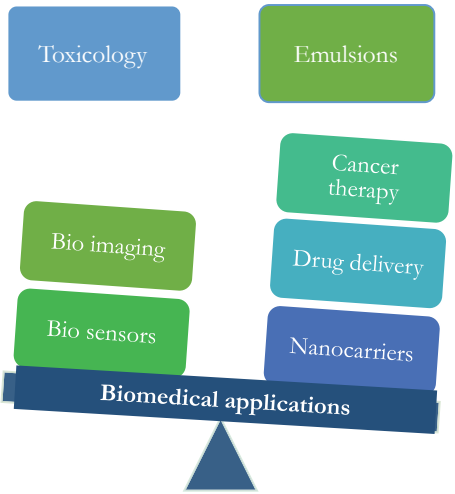

Fig. 1 An illustrafftion of some biomedical applications involving nanoparticles

2 Nanotechnology in Biomedical Applications

It is noted that many changes are needed for the transformation of a discipline from life science to technology and its applications. This development must involve Innovative design and simulation implementation, the potential to assess and evaluate, and extensive initiative in the advancement of technology. In life science, the functions and actions of a body, including cells, RNA, and DNA or Proteins, are on the nanoscale level. Thus the use of nanotechnology is the gateway to biotechnological progress [19]. Ultimately, nanotechnology can make it possible to transport and manipulate biomaterials and integrate them [20]. In biotechnology, nanotechnology has special applications, particularly in diagnosis and therapeutics [21]. It is possible to combine various biological compounds with nanomaterials using physicochemical processes and through particular biochemical reactions, such as Protein-protein interactions, antibody-antigen interactions [22]. The focus on using nanomaterials in biomedical applications, such as drug delivery, hypoxia, therapy, biosensors, and bioimaging, is increasingly gaining popularity [23] (Fig. 1).

3 Properties Involved in Biomedical Applications

3.1 Magnetic Property

The most frequently studied and widely applied material for biomedical applications are magnetic nanomaterials. Its effectiveness is attributed to specific structural, chemical, and magnetic properties like stability, non-poisonous, bioactivity, high magnetic

flux [24]. These Magnetic nanoparticles are mostly comprised of Fe_3O_4, Fe_2O_4, Co-doped Fe_2O_4, and Mn-doped Fe_2O_4. These nanomaterials are most studied since they all have unique characteristics which are crucial for use in various medical applications, like selective delivery of drugs, bioimaging, magnetic hyperthermia, therapy, biosensors, and photoablation [25].

3.2 Optical Property

The optical properties of metal oxide nanoparticles are mainly focused on biomedical applications. Doped materials are excellent frequency converters covering the spectrum from ultraviolet (UV) through visible to near-infrared because of the distinctive electronic structure of transition metals. The probability of biomedical application is a further benefit of the optical approach, gaining the benefit of different absorption spectra. Metal oxide-based NPs attract growing attention as optical sensor indicators and therapeutic and diagnostic agents from the biotechnology, chemistry, optics, and biomedical community due to their optical properties [26, 27].

3.3 Surface Morphology

The selective behavior is encouraged by this surface arrangement through increasing the active spots, leading to biomolecules being spread across the surface. By reducing steric interference and improving accessibility to the binding sites, biomedical applications are carried out on this sort of surface. It relies on the fact that the thermodynamic and kinetic mechanisms of the surface active sites and analytes have the same order, allowing for more efficient biomedical behavior. Ultimately, when the surfaces are structured geometrically, this reflects unique optical and electric properties which are used in improving various applications like high functional bio-implants, efficient biosensors, biochips in neuronal computing, Medical diagnostics with accuracy, molecular separations, and biosynthesis [28].

4 Nanoparticles in Biomedical Application

4.1 Drug Delivery Systems

Lately, major developments have occurred in this area of drug carriers systems to deliver drugs to their specified location for treating the different health conditions. A number of new drug delivery technologies have been widely implemented. However, there are some issues to be resolved. Therefore the nano-based drug carriers which

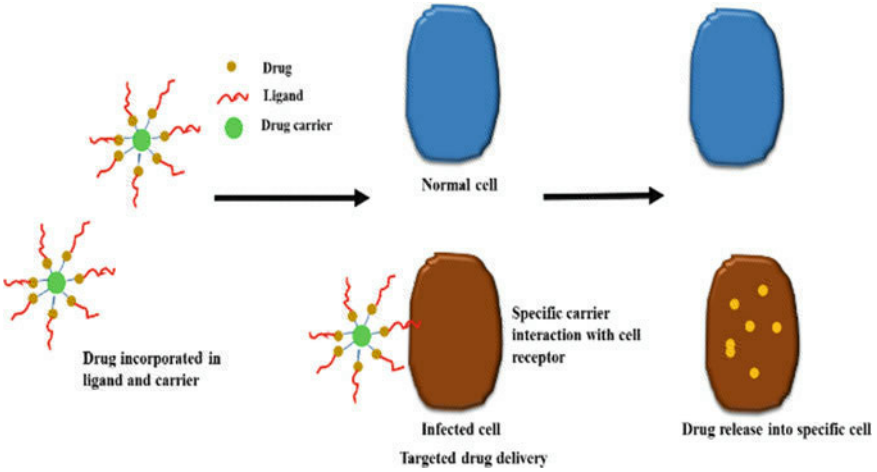

Fig. 2 Schematic representation of targeted drug delivery

will facilitate the highly developed drug delivery system are studied effectively [29]. This is due to its positive effects, like the capacity to change characteristics like solubility, patterns of drug release, diffusability, bioavailability, Suitable paths of administration, reduced toxic effects, lesser side effects, enhanced cellular uptake, and prolonged life cycle of medications and tolerability [30] (Fig. 2).

4.1.1 Polymeric Nanoparticles

Polymeric nanomaterials have more excellent biocompatibility with effective functional groups [31]. It's used in the binding or coating of nanomaterials of different sorts. Therefore, multiple nanoparticles of various functions are formed for effective use in the identification and treating the multiple forms of diseases. Xiaoping et al. [32] showed that a sequence of nanosized amphipathic cetirizine-chitosan polymer was efficiently used as a mucosal drug delivery system. In the presence of lysozyme, Cetirizine dihydrochloride (CedH): chitosan NPs demonstrated burst and persistent levels of drug release, with no major negative impacts on the body fluids [32]. Talitha et al. developed a chitosan film carrying PLGA nanoparticles packed with enhanced flavonoid fraction of *Cecropia glaziovii*. The result showed that the efficient chitosan nanocomposites were synthesized with an efficient capacity to overcome the less availability issue of EFF-Cg and proved as the potent delivery system in treating herpes infection [33]. Zhao et al. [34] discussed that the Glucose-sensitive polymer nanoparticles coupled with glucose oxidase, concanavalin A, and phenylboronic acid for self-controlled delivery of drugs which can give better control of blood level, and also delivers a precise dose of the medicine (e.g., insulin), Copying the pancreas' physiological control. GOD, Con A, or PBA [35]. Similarly, there are numerous

polymeric nano drug carriers whose efficiency and the target application are listed in Table 1.

Table 1 Polymeric nano drug carriers with the target applications

Sl. No.	Polymer nanocomposite	Drug carried	Outcome	References
1	Tetraphenylethylene immobilized zirconium-based nanoscale coordination polymers	Curcumin	Promising medium for efficient delivery of drugs and continuous image analysis of fluorescence	[33]
2	Poly(lactic-co-glycolic acid)	Dox-HCl Dox-base	Enhanced hydrophilic drug miscibility in a hydrophobic PLA polymer will decrease the rate of discharge	[35]
3	NCPs, which consist of manganese ions (Mn^{2+}), as the metal connecting points, and dithiodiglycolic acid, as the organic bridging ligands	Doxorubicin	Enhanced in vivo inhibitory effects of tumor growth compared to free DOX	[34]
4	SiO2-PMAA-b-PNIPAM	Doxorubicin	DOX-loaded SiO2-PMAA-b-PNIPAM nanoparticles are Extremely effective towards Hela cells	[36]
5	Cellulose nanocrystals-HPG-HEBA	Epirubicin	Successfully accepted by cells, EPI nevertheless retains its biological activity for Attack of cancer cells	[37]
6	Oligo(ethylene glycol) methacrylate	Doxorubicin	Promoted drug release at pH 5.0, greater cellular uptake and cytotoxicity of Dox-loaded pH-sensitive micelles of PCL21-b-P(a-OEGMA)11 relative to the pH-insensitive analogs of PCL21-b-P(OEGMA)18	[38]
7	Polymer coated silica nanoparticles modified with guanidine containing co-polymers—γ-Fe_2O_3	Molsidomine	High capacity for drug loading because of the efficient electrostatic interactions of guanidine and molsidomine Which consists co-polymers	[39]

4.1.2 Metallic Nanoparticles

Metal-organic composites are flexible classes of hybrid materials made by metal comprising structures bound by organic linkers in three dimensions. A good number of different metallic nanoparticles with organic framework provides a wide range of properties that allow them to be useful in numerous applications including drug delivery. Due to several properties, like high pore size distribution and volume, they are becoming ideal for delivery of drugs. The capacity to modify organic linkers for stealth-tracking or biocompatibility, besides the higher carrying ability, indicates that changes can be made to metallic nanoparticles which are well developed to deliver drugs [40, 41].

Siamak et al. [42] synthesized carboxymethylcellulose/Zinc-based metal-organic framework/graphene oxide bio-nanocomposite to carry doxorubicin. The DOX release rate was considerably greater in the tumor cell pH 5 than in physiological conditions at pH 7.4. Also, the analysis suggests that DOX@CMC/MOF-5/GO exhibited substantial K562 cell cytotoxicity [42]. Wang et al. [43] showed that the mesoporous $FeSe_2$ hedgehogs can be tailored and used for tumor therapy using doxorubicin. Because of FeSe2 hedgehogs' powerful NIR-II photothermal activity, 1120 nm light irradiation into tumor cells leads to gelatin melting, regains the spiky structure, and thus promotes internalization of cells, this results in a particular aggregation in the tumor cells [43]. Zied et al. [44] Synthesized magnetic nanoparticles composed of iron oxide, 2-(2-methoxy)ethyl methacrylate (MEO2MA) and oligo(ethyleneglycol)methacrylate (OEGMA) for enhanced delivery of 100% doxorubicin after 52 h at 42 °C [44]. Milad et al. [45] stated that the prepared gold-iron oxide nanocomposites can be it will be used as a viable transport for Lipoic acid-curcumin (LA-CUR) a novel anticancer drug. Being a negatively charged carrier, studies showed a substantially increased cytotoxicity toward cancerous U87MGG in contrast to curcumin [45]. Carbon/calcium phosphate/Fe3O4 composite nanoparticles synthesized by Mingyu et al. can be rendered as a transverse relaxation (T2) contrast agent for MRI and when the cells are treated with carbon/CaP/Fe_3O_4, cell viability is as great as 95.6% demonstrating the composite NPs showed superior cytocompatibility [46]. There are diverse metallic nano drug carriers whose efficacy and target output are described in Table 2.

4.2 Biosensors

Nanobiotechnology implies methodologies that integrate nanomaterials or nanoparticles to build tools for biological processes as given in Fig. 3. As the active elements laid the groundwork for a major advance in the area, resulting in stable sensor devices, nanomaterials are integrated into the sensor applications. With their flexible surface chemistry, optoelectronic merits, the manufacturing processes, coupled with morphological characteristics, nanomaterials are by far the most frequently used in biomedical research [53, 54]. Usually, an electroanalytical biosensor comprises two main

Table 2 Metallic drug carriers with the target applications

Sl. No.	Metallic nanocomposite	Drug carried	Outcome	References
1	Gadolinium oxide-gold nanoclusters hybrid	Indocyanine green (ICG)	High loading capacity for the drug of 1.74 g/g	[47]
2	MIL-88A NPs composed of iron(III) and fumaric acid	Suberoyl bishydroxamic acid	strong therapeutic capacity without any early leakage when coated using exosome	[48]
3	UiO-66, a zirconium-based Metal–organic frame work	model cargo, RhB, and a corticosteroid, dex	UiO-66 NPs are a modern aerosol platform for a vast array of lung diseases, which include COPD, lung cancers and COVID-19, with possible targeted delivery	[49]
4	Multifunctional magnetite mesoporous silica nanoparticles	Tamoxifen	Research indicates that the highest biocompatibility of nanogels after 72 h is well above 80% viable cells	[50]
5	Zinc(II) metal–organic frameworks (Zn-MOFs)	5-FU and DOX	22.5% and 26.72% of DOX were released from the NPs after 12 and 24 h at pH 7.4, while 47.92% and 55.1% of the drug were released in the same time at pH 5.5, respectively	[51]
6	ZnO quantum dots	Doxorubicin	Could be fully biodegraded in the acidic environment, with almost 72% of DOX discharged after 80 h	[52]

sections. The analyte-recognizing biological factor in the sample. The segment of the detector that transforms the signal produced into a signal from biological activity, that can be calculated more effectively [55].

Qingzhou et al. synthesized In_2O_3 nanoribbon modified with the enzyme glucose oxidase, chitosan, and carbon nanotubes (SWCNTs) for glucose detection in various body fluids, such as sweat and saliva. This showed a mobility of $\sim 22\ cm^2\ V - 1\ s - 1$ in $0.1 \times$ saline buffered using phosphate. It's been affixed on different

surfaces, including watches and synthetic arms [56]. Hamed et al. [57] prepared a hydrogel by copolymerizing PEG linker and polyethylene glycol and to activate covalent cross-linking and gel formation, Eosin Y is taken as the photoinitiator. In order to efficiently facilitate the enzymatic reaction causing penicillin tracking down to 0.2 mM, the hydrogel-mediated activation of penicillinase was explained. To accomplish extremely accurate sensing, multiplexed surface modification was shown with penicillinase and acetylcholinesterase [57]. Montmorillonite clay was binded using PAMAM G2 dendrimers by Betul et al. and electrospinned using poly(vinyl) alcohol and pyranose oxidases. The identification limit was 0.7 μM glucose [58].

Samira et al. showed that iron (III) in the presence of 1, 10-phenanthroline detects hydroquinone and Catechol in the limits of 0.05 and 0.07 mg L-1. The linear dynamic range was 0.5–3.0 mg L−1 for both analytes [59].

4.3 Antibacterial Agents

Nanoparticles are usually able to interact with microbes as an effective antifungal and antibacterial agent. In recent years, the progress of nanotechnology has facilitated the discovery of new antibacterial drugs. In relation to traditional materials, as the size of materials reduces from micrometer to the nanometer scale, nanomaterials exhibit higher efficiency, like improved diffusivity, excessive material strength and chemical reactivity, and improved biological activities. Usually, through various forms of gram-negative and positive strains of bacteria, the antibacterial efficiency of nanoparticles is achieved [60]. This may be due to the occurrence of Reactive oxygen species generated, protein damage, DNA damage, Mutagenesis, Enzyme disruption, membrane damage, or destruction of electron transport [20] .

In order to battle pathogens, metals have been around since earlier times. Because of its wide inhibitory range towards microbes and pathogens, metal nanoparticles have gained increased curiosity as antimicrobial agents [61]. Qing et al. [62] proved that the synthesized copper nanoparticles damage Escherichia coli as high as 86.3 ± 0.2% within 12 h at the dosage of 100 μg/mL. The main explanation for the behavior is the production of oxygen radicals that destroys the constituents of the cell membrane and cytoplasm and inactivates lipid peroxidation and DNA damage [62]. By using a green synthesis technique, Tu Uyen et al. synthesized ZnO NPs using orange-peel extract as the reducing agent. The antimicrobial rate in the direction of *E. coli* was over 99.9%, while the bactericidal rate against Staphylococcus aureus in the relatively large range of 89–98% [63]. Dongdong et al. [64] synthesized remarkably effective antibacterial towards drug-resistant Escherichia coli (*E. coli*) and Staphylococcus aureus (*S. aureus*) are displayed by silver-decorated quercetin. Disruption of Nucleic acid assay presumed that the expression levels of DNA from both species steadily reduces with the concentrations of QA NP. Gene expression screening like RNA Seq is used to assess the sensing of toxicity pathways [64]. Shamkumar et al. [65] synthesized Ag NPs−PANI/MWCNT resulted in bacterial inactivation because of

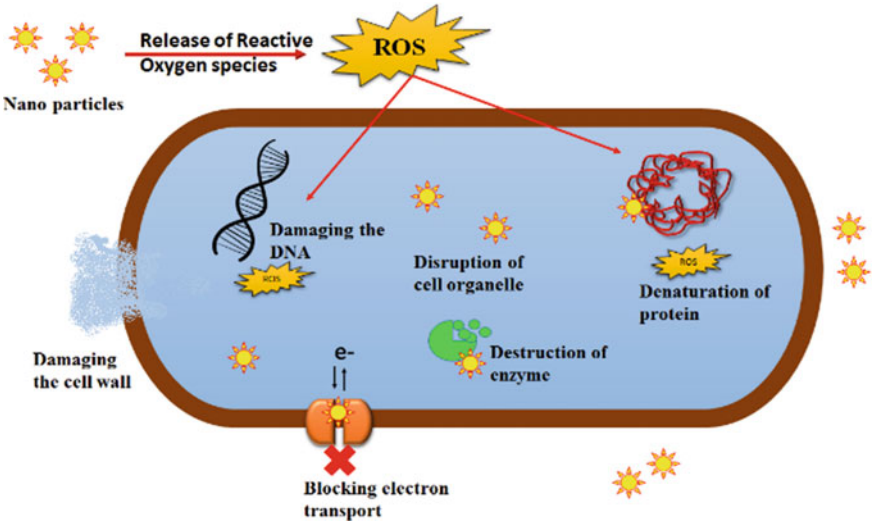

Fig. 3 Schematic diagram showing the mode of antibacterial activity

higher surface area of Ag NPs, and 1D MWCNT and acidic functional group of PANI [65].

Sl. No.	Nanomaterials	Bacterial strains	Report	References
1	Povidone-iodine nanoparticles	*E. coli* *S. aureus* *P. aeruginosa*	Iodine was mounted on P(NVP-MMA) NPs, with a contact period of 30 min displaying 100% elimination of E coli and S aureus	[66]
2	ZnO and CuO capped with polyvinyl alcohol, polyethylene glycol, and polyethylenimine	*E. coli* *S. aureus*	After 120 min of exposure, 99.9% bacterial destruction was exhibited by CuO-PEG and ZnO-PVA	[67]
3	Chitosan/Pd nanocomposites	*S. aureus* *B. anthracis* *B. subtilis* *B. cereus* *P. aeruginosa* *K. pneumoniae* *E. coli* *Proteus sp.*	Mic was recorded for CS/Pd-15%, i.e., 0.78, 1.56, 6.25, 0.78, 25, 50, 25, 0.78 μg/ml respectively	[68]
4	Ru(II) polypyridine complexes	*E. coli* *S. aureus* *Enterococcus*	16, 8, 16 μg/ml Mic were recorded respectively	[69]

(continued)

(continued)

Sl. No.	Nanomaterials	Bacterial strains	Report	References
5	Silver nanoparticles on mesoporous graphene	*E. coli*	When exposed for 2 h and showed an inhibition zone of 0.42 cm achieving 100% removal	[70]
6	Au–Ag NPs	*E. coli* *S. aureus*	Larger inhibition zone for *E. coli* and *S. aureus* 36.4 mm and 35.3 mm in average diameters, respectively	[71]
7	Tungsten oxide-graphene oxide	*E. coli* *B. subtilis*	Maximum inhibition at 2.5–5 mg/mL at irradiation for 6 h	[29]
8	Titanium dioxide	*E. coli* *S. aureus*	The minimum inhibitory concentration of 25 mg/mL^{-1} and 50 mg/mL^{-1} respectively	[72]
9	Au@Ag NPs	*E. coli* *S. aureus*	Minimum inhibitory concentration are 5 mg/mL^{-1} for *E. coli* and 7.5 mg/mL^{-1} for *S. aureus*	[73]

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Chapter 2
Lipid Nanocarriers: Applications in Biomedical Research and in Drug Delivery

Sujata Maurya, Manish Kumar Mishra, Brijesh Rathi, and Dhruv Kumar

1 Introduction

Lipid nanocarriers are the most advanced non-viral drug delivery systems. They are called nanocarriers, because of their size which is about few nanometres only. Nowadays, it is no doubt that nanoformulations are of extreme advantage in the arena of pharmaceutics. Lipid nanocarriers have become indispensable for use as drug delivery systems because of their complete biocompatibility and nontoxic nature [1]. There are numerous studies proving the safety and high efficacy of lipid nanoparticles in the fields of pharmacology, diagnostics, nutraceuticals, etc. Such studies have been the impetus in further research and development into this arena of nanoscience. Solid lipid nanocarriers (SLN) were the first generation nanocarriers. There were many advantages of SLN, but since the SLN is formed of a crystalline solid so it has a capacity to form gel, low incorporation rate. SLNs could not deliver the drug efficiently to the target site [2]. Due to the inefficacy of SLNs, NSL (nanostructured lipid carriers) were formulated. To overcome the disadvantage of solid lipid nanoparticles these lipid nanocarriers are formed of solid and liquid lipids. This possibility of drug incorporation in the lipid nanocarriers is a new technique which is highly advantageous and bio risk free. Oral administration of lipid nanocarrier based drugs

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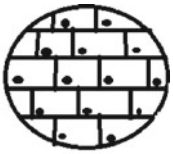
is also possible, other traditional forms of sachets, tablets, etc. are also available. The major application of the ultra-deformable nanovesicles is their ability to transfer the drugs across the natural mammalian skin barrier. Various unstable proteins, peptides, drugs, and vaccines are transferred efficiently [3] (Figs. 1 and 2).

The major challenge faced by these lipid nanocarriers is that they cannot be administered by the parenteral route of drug administration because these are then recognized as foreign by the cells of reticuloendothelial system. This challenge can be overcome only if the size of nanoparticle is even smaller than 200-micron meters because these size nanocarriers are not treated as non self by the cells of RES.

Solid lipid nanocarriers (SLN) and Nanostructured lipid carriers (NSL)

Solid Lipid Nanoparticles (SLN)		• SLN is a perfect crystal lattice structure. • There is less space for accommodation of drug inside the lipid core, resulting in the less drug loading and expulsion of drug out of the system.

Nanostructured Lipid Carriers (NSL)

NLC Type I		• It is an imperfect crystal core. • More space is available for drug accommodation inside the lipid core. • Hence, higher drug loading is possible and reduced/no possibility of drug expulsion from core.
NLC Type II		• This type is also known as structure less type. • Instead of conversion into a crystalline structure, solid lipids incorporated into this get converted into an amorphous form.
NLC Type III		• This is multiple model known as O/F/W model. • Drugs having higher solubility in liquid lipids/ oils than solid lipid can be formulated into this type. • It can be prepared by phase separation method. • Drug is present in the dissolved state inside tiny oil droplets and uniformly distributed in the solid core.

Fig. 1 Shows the structures of SLNs and different types of NLCs [3]

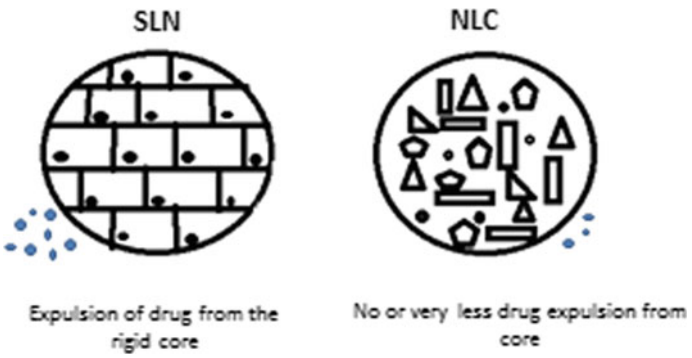


Fig. 2 Stability profile of SLNs and NLCs [5]

There remains a lot of research that must be carried out further in this field of nanotherapeutics [4].

The main advantages of lipid nanocarriers over the conventional carriers are as follows [6]:

1. Can store and extendedly release the target drug
2. Can store and release the target drug in an efficient and a stable manner
3. Both lipid soluble and water-soluble drug carriers
4. Most of the lipids used in formulation of lipid nanocarriers are biocompatible and non-allergens
5. Their production can be easily upscaled and are very easy to sterilize also.

Various lipid molecules interact with each other leading to formation of lipid-based nanostructures, which have no nonspecific interaction with other biomolecules, which in turn makes them a promising model for use in human body systems [7]. Lipid nanocarriers are one of the devices which have resulted out due to another revolution in the field of nanotechnology (Table 1).

Table 1 Differentiating parameters of SLNs and NLCs (Salvi and Pawar, 2019)

S. No.	Parameters	Solid lipid nanoparticles	Nanostructured lipid
1	Nature of lipids	Solid	Blend of solid and liquid lipids
2	Possible drug accommodation	Low	High
3	Degree of crystallinity	Higher (ordered matrix)	Lower (Amorphous/imperfect crystalline matrix)
4	Drug escape from matrix in dispersion media	Comparatively higher	Lower
5	Stability	Lower	Comparatively Higher

1.1 Classification

Different types of lipid nanocarriers are classified as follows:

1. Liposome
2. Transferosomes
3. Ethosomes

2 Liposome

2.1 Introduction

The first demonstration of liposome preparation was given by Prof. Alec Bangham [8], in Babrahm Institute, Cambridge, England in 1965. Since their discovery, the liposomes have been used as drug and pharmaceutical carriers (Fig 1). The liposomes consist of a central aqueous space (03–10 micrometer in diameter) surrounded by lipid bilayer comprising amphipathic lipids or phospholipids. So, basically, liposomes are nano sized lipid moieties of spherical shape [9]. There has been a lot of progress in the research on liposomes from conventional spherical liposomal bodies to second generation liposomes [10].

Second generation liposomes are those in which the size, charge, and composition of a lipid molecule are altered to some extent so as to make it a better delivery agent. Liposomes are nowadays widely used as drug delivery systems (for, e.g.,- doxorubicin, daunorubicin, cytarabine, etc.) for treatment of various infectious diseases and cancers also (Fig. 3). There are many advantages and disadvantages of using liposomes which are summarized in Table 2.

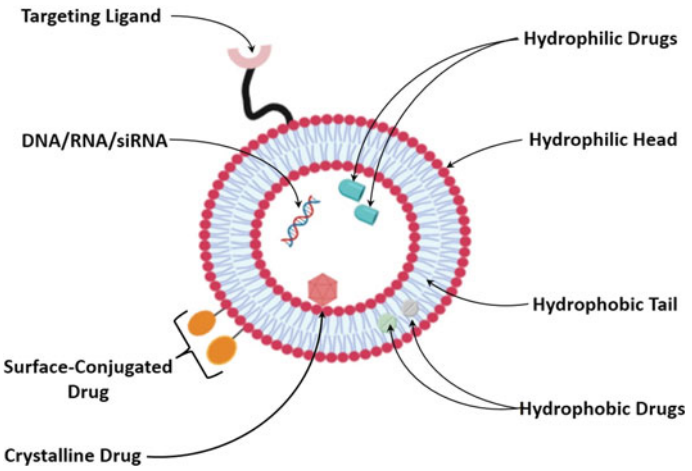


Fig. 3 Basic structure of a liposome drug delivery system

Table 2 Advantages and disadvantages of liposomes [11]

S. No.	Advantages of liposomes	Disadvantages of liposomes
1	Liposomes increased efficacy and therapeutic index of drug (actinomycin-D)	Low solubility
2	Liposome increased stability via encapsulation	Short half-life
3	Site avoidance effect	Fewer stables
4	Liposomes help reduce the exposure of sensitive tissues to toxic drugs	Production cost is high
5	Liposomes reduce the toxicity of the encapsulated agent (amphotericin B, Taxol)	Leakage and fusion of encapsulated drug/molecules

2.2 Composition

Liposomes formulation majorly consists of two types of phospholipids- glycerophospholipids and sphingomyelins. Glycerophospholipids (glycerol as backbone) and sphingomyelins are mainly the constituents of eukaryotic cells. The structure of a liposomal entity can be varied by altering the head groups of the glycerophospholipids. The different head groups can be phosphatidylcholine, phosphatidyl serine, phosphatidylethanolamine (Table 3), sphingomyelins have the property of efficient molecule entrapment, high stability in serum, also are readily released after delivery of the molecule to target organ [12].

2.3 Methods for Preparation of Liposomes

Three to four basic steps for liposome formation are as follows:

Step 1:- Lipid drying through organic solvent evaporation.
Step 2:- Dispersing the dried lipid in aqueous medium.
Step 3:- Involves the purification process of the obtained liposome
Step 4:- To structurally analyze and characterize the formed liposome.

Table 3 Liposome classification based on composition and mode of drug delivery [13]

S. No.	Type	Composition	Characteristics	References
1	Conventional liposome	Neutral and or negatively charged phospholipids + cholesterol	Subject to coated-pit endocytosis, contents ultimately liposomes delivered to lysosomes if they do not fuse from the endosomes, useful for RES targeting; rapid and saturable uptake by RES; short circulation half-life; dose dependent pharmacokinetics	[14]
2	PH sensitive	Phospholipids such as phosphatidyl ethanolamine, dioleoyl phosphatidyl ethanolamine with either CHEMS or OA	Subject to coated-pit endocytosis at low pH, fuse with liposomes cell or endosome membrane and release their contents in cytoplasm; suitable for intracellular delivery of weak base and macromolecules; biodistribution and pharmacokinetics similar to conventional liposomes	[15]
3	Cationic liposomes	Cationic lipids	Possibly fuse with cell or endosome membranes; suitable for delivery of negatively charged macromolecules (DNA, RNA); ease of formation; structurally unstable; transfection activity decreases with time; toxic at high dose, mainly restricted to local administration	[16]
4	Temperature (or) heat sensitive liposomes	Dipalmitoyl phophatidylcholine	Vesicles showed maximum release at 41°Y, the phase transition temperature of dipalmitoyl phophatidylcholine. Liposomes released the entrapped content at the target cell surface upon brief heating to the phase transition temperature of the liposome membrane	[17]

(continued)