Chapter 3

Bioinspired Nanomaterials for Drug Delivery

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Abstract

Over the preceding few decades therapeutic/drug delivery systems were explored and investigated as a tactic to advance the efficiency and safety of therapeutic agents for various biomedical applications. Nano-engineering on the various biomaterials are reported and are under investigation to enhance the pharmacokinetics and pharmacodynamics of many drugs, with proven enhancements in terms of objective facility, therapeutic efficacy, reduction in dosing frequency and associated drug side effects. Bioinspired materials from various sources (biomass, plants, animals, cells, biotechnology interventions) are of great interest with additive advantages over synthetic materials in terms of biocompatibility, biodegradation, nontoxicity, non-immunogenic and are cost effective systems. Bioinspired nano platforms are proceeding round the world to contrive novel drug delivery carriers using different strategies. This chapter encompasses encroachments in the diverse types of bioinspired polymers and their nano delivery systems. Comprehensive evidence is also concise on delivery systems morphological, biological functionalities from respectively material and their potentialities as persuasive carriers for drug delivery systems.

Keywords

Nanomaterials, Nanodelivery Systems, Nanoparticles, Nanotherapies
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1. Introduction

1.1 Bioinspired biomimetic materials

Although many therapeutics show high pharmacological activity toward specific pathologies, their use in the native form is often limited by practical reasons. Major drawbacks associated to free drug administration are related to the poor stability, limited biodistribution, low barrier penetration capabilities and lacking targeting properties of active molecules. Cited restrictions have pushed the introduction of nanoscience in medicine, with the development of nano-sized controlled drug delivery systems.

Nanoparticles for drug delivery effectively reduce hurdles of free drug administration, promoting the use of existing drugs, already developed and tested, but unused in free form for their induced side effects, with a significant reduction of costs related to drug discovery. Nanoparticles are homing systems that hide and protect poorly stable active molecules from physiological environment, preserving the pharmacological activity. Additional benefits associated to nanoparticles in drug delivery are related to their customizability and functionalizability, which provide specific properties to address poor bioavailability, issues related to solubility and the off target deposition in healthy tissues.

In recent years, the exploitation of nanoparticles, from synthetic or biological derivation, or biohybrid, is significantly widespread, thanks to significant benefits that vectors can provide.

At first, materials for natural derivation were processed to obtain carriers for drug delivery. Natural materials, from plants (e.g., alginates) or animals (e.g., chitosan), were extensively used for their degradability and biocompatibility. Also liposomes were considered valuable carriers to entrap and transport drugs. Liposomes can be obtained from amphiphilic natural molecules by means of well consolidate procedures. Preparation procedures for carriers from natural derivation were optimized for a wide range of starting materials, architectures and final dimensions. Although their functional
behaviour was acceptable, natural carriers were successfully improved by introducing chemical modifications and then obtaining hybrid materials.

The development of hybrid materials pushed the discovery of novel and more performant synthetic polymers that were, in consequence, evaluated as starting materials for carrier preparation. Artificial drug carriers, composed of degradable polymers or inorganic materials, are constantly under investigation and achieved good results pushed a number of systems into the market. Natural and artificial particles represent the first generation of drug carriers. The basic concept for the design of first-generation nanoparticles was to provide a homing system for active molecules, to protect therapeutics from the physiological environment and modulate the delivery kinetics.

However, synthetic nanoparticle can be modified and functionalized to improve stealth and targeting properties. Such novel characteristics led scientists to develop more complex systems, with engineered surfaces, decorated with natural molecules or synthetic bioinspired units. Beside synthetic nanoparticles, natural systems derived from pathogens or cells possess suitable properties to improve drug therapies. Biological vectors have intrinsic characteristics enabling long circulation and targeting of specific districts. Natural vectors evolved over years to accomplish their tasks, refining their peculiar characteristics. Scientists have now developed specific protocols to obtain safe carriers from living cells, as well as improved techniques to maximize drug loading without compromise, native carrier properties ghost or living cells are currently under investigation with interesting results. While functional properties of natural and artificial nanoparticles are well known and already optimized with consolidate strategies [1], functional performances of biological systems are not yet well recognized [2]. Moreover, the increasing advances in cell biology allow today to merge beneficial aspects of all classes, to obtain combined biohybrid structures with improved characteristics.

1.2 Nano engineering of biomaterials and their biomedical applications

Nano engineering of nanomaterials with diverse sources are used to accomplish nanocomposite. Carbon-based nanomaterials (carbon nanotubes or CNTs, graphene, nanodiamonds), polymeric nanoparticles (dendrimers and hyper branched polymers), inorganic/ceramic nanoparticles (hydroxyapatite, silicates and calcium phosphate) and metal/metaloxide nanoparticles (gold, silver and ironoxides) are specific instances of these nanomaterials (Figure 1). This integration adds unique properties into hydrogels including the following [3]:

- The biomaterials are principally used for implantation solicitations such as dental implant, mechanical heart valve, intraocular lens, hip, knee and shoulder joints, etc.
• They remain similarly used to nurture cells in culture, to assay for blood proteins in the clinical laboratory, in equipment for dealing out biomolecules for biotechnological presentations, for implants to normalise fertility in cattle, in diagnostic gene arrays, in the aquaculture of oysters and for investigational cell-silicon “biochips”.

• The bioactive ceramic Nano-sized Hydroxyapatite (HA) is available commercially for use in bone replacement applications. HA [Ca10(PO4)6(OH)2] is a synthetic calcium phosphate material that has similarities to the mineral component of human bone.

• The nanosized biomaterials can also diminish the drug-release rate, revealing sustained releasing actions. Decisively, the rational particle size and spherical morphology bequeath with intravenous transport capability. Nano-biomaterials are considerably further seemly for the encapsulation and delivery of hydrophobic therapeutic agents because the carbonaceous framework and also can form specific π-π supramolecular interactions with aromatic drug molecules.

• Photothermal therapy (PTT) has remained broadly pragmatic to indulgence cancer by using NIR-resonant nano-agents, which might absorb the NIR light and transform it into cytotoxic heat to kill the cancerous cells and cut the invasive impairment to normal cells.

• Hyaluronic acid (HA) functionalized undeviating mesoporous carbon spheres (UMCS) were fashioned for targeted enzyme amenable drug delivery disbursing a facile electrostatic attraction approach.

• Gene therapy is assumed to be an operative and benign mode to overwhelm oncogenes and confine the proliferation of intractable tumors through emerging exogenous nucleic acids as therapeutic agents. Polyethylenimine (PEI) revised oxidized mesoporous carbon nanosphere (OP) for combined photothermal and gene therapy.
1.3 Advantages of bioinspired materials

Advantages of nanoscience and nanotechnology have overwhelmingly headed to the improvement of functional materials in current years, which obligate institute solicitations extending from biomedical to ecological engineering and high-energy storage as well as gathered benefits in fundamental science. Amongst these efficient nanomaterials are carbon nanotubes (CNTs), graphene, fullerenes, soft, polymeric nanoparticles, metal organic nanomaterials, self-assembled and supramolecular nanostructures, and their results to label a little. Their exceptional physico-chemical properties such as catalytic, dielectric, optical and mechanical give rise to their distinct solicitations in sensors, drug delivery, proteomics and biomolecular electronics. In exact, their biological solicitations have expanded fundamental indulgent of biomolecular systems such as vesicles, viruses and cells as well as enthused the intention of nanomaterials with biological functions. The former ones obligate been frequently called bioinspired nanomaterials [4].

1.4 Advanced bioinspired nanodelivery systems

Inspired by nature's astonishing delicacy, scholars obligate remained scheming nanomaterials with variability of solicitations in biomedicine. The principal intention for
the astonishing utilities of these bioinspired nanomaterials stems from the point that the human biological structure is made up of nanoscale self-assembly of biological molecules. There has remained notable evolvement in the earlier decades in the area of biomimics and bioinspired materials such as organs-on-chips, smart robotic devices, a new class of materials that mimic the homeostatic skills of living organisms to acclimatise and self-regulate, and nanomaterials for tissue engineering and orthopaedic implants. Biological models are architectures that execute as vessels such as viral capsids. Explicitly, these biological containers can utility as carriers for DNA assays and immunoassays, drugs, catalysts, and be used in novel material synthesis [5].

2. Advanced bioinspired nano delivery systems

2.1 Albumin based nano drug delivery systems

Albumin is the furthermore profuse form of serum protein frequently institute in the blood; albumin is diverse from further plasma proteins since it is not glycosylated. Crucial benefits of albumin-based targeting carriers embrace biodegradation, non-immunogenicity, and significant stability over a wide range of pH (4–9) and temperature (10–60 °C). Albumin retains a cryoprotectant outcome, which is practicable for lyophilization of formulations; it also has a long half-life, which is required for prolonged renal clearance. Furthermore, albumin can conveyance a variability of molecules and plays a crucial role in sustaining homeostasis [6]. As such, albumin is deliberated an ultimate carrier component to enrich pharmacokinetic profiles of various drugs. Approaches have remained advanced to synthesize albumin-based drug carriers by binding or conjugating drug cargos to endogenous or exogenous albumin. A paclitaxel bound albumin nanoparticle is a model example for instituting the probable of albumin-based delivery. It binds to the gp60 receptor extant at the cell surface and activates caveolin-1 mediated transcytosis, which also transports some of the unbound plasma constituents. This system can be subjugated for transporting the cargo to the brain via adsorptive mediated transcytosis. Moreover, the albumin-bound paclitaxel had a ~4-fold increase in the cellular uptake of endothelial cells as paralleled to clinical formulation [7].

2.2 Examples of bio-inspired delivery systems in clinical trials

Albumin has turn into one of the utmost imperative drug delivery carriers in cancer therapy [6]. Numerous albumin-based products have prepared it to clinical trials or level commercial claims. For example, INNO-206, an albumin bound prodrug, is enduring Phase I clinical trials for treating sarcoma and gastric cancer. This is an acid-sensitive hydrazone imitative of DOX, retentive high plasma stability in its albumin bound form
and dropping cardiotoxicity of DOX. Abraxane produced by Celgene is another well-established albumin-based paclitaxel nanoparticle system used for treating solid tumors. This product has confirmed lower toxicity and higher antitumor efficacy than unbound paclitaxel [8].

2.3 Polysaccharide based nano drug delivery systems

Carbohydrates, sometimes called “sugars,” are an imperative class of biomolecules found profusely in nature. Monosaccharides, the simplest sugars, are the basic structural units of carbohydrates. These units have three to nine carbons and a distinguishing carbonyl group, which can be moreover an aldehyde, in aldoses, or a ketone, in ketoses. Monosaccharides occur predominantly in cyclic form, and can be linked together via “α” or “β” glycosidic bonds, forming linear or branched chains of oligosaccharides (2–20 units), with the general formula (CH2O)n.

Chains with more than 20 monosaccharide residues are stated to as polysaccharides. The generic term “glycan” is frequently used to denote to any oligo- and polysaccharide, either free or covalently linked to other molecules, such as proteins or lipids, in the form of glycoconjugates. The field of glycobiology has been emerging at a prodigious step over the past decades. Though carbohydrates were principally deliberated principally as storage and structural materials, it is currently clear that they reveal a plurality of biological activities [9]. This is in large part accompanying with their excessive diversity, for which quite a lot of factors subsidize. There is an inclusive array of monosaccharides. The ones frequently institute in animal glycans embrace: (i) neutral sugars pentoses and hexoses; (ii) hexosamines hexoses with a free or N-acetylated amino group; (iii) deoxyhexoses hexoses without a hydroxyl group at position (iv) uronic acids hexoses with a negatively charged carboxyl group; and (v) sialic acids family of 9-carbon acidic sugars [10]. Apart from the previously stated adaptations, hydroxyl groups of monosaccharides can also be chemically revised by methylation and esterification (phosphate, acyl, and sulfate esters). Furthermore, the existence of asymmetrical (chiral) carbons in monosaccharides gives rise to diverse isomeric forms, with diverse biochemical properties. To practice higher-order structures, mono-saccharides can be linked organised in many diverse ways, because of the several potential isomers. Bioinspired Materials for Medical Applications that can be designed between two units. The glycosidic linkage can encompass substitute stereoisomers (α or β) at the anomeric carbon of the earlier unit, and the several hydroxyl groups at the ensuing unit consent several potentials of isomerization. The collective existence of diverging also subsidizes to the structural diversity of glycans. This way, provisional on the type of glycosidic linkage, sugar chains of alike alignment can adopt very diverse conformations and
bioactivities. A classic example is that of starch and cellulose, which are both homopolymers of glucose found in plants, where they play storage and structural roles, respectively. While α1 4 linkages and branching in starch outcomes in helical chains and a added disordered three-dimensional (3D) structure, β1–4 linkages in cellulose result in a straight chain 3D structure, strengthen by interchain hydrogen bonds. These structural adaptations explanation for their quite dissimilar biochemical properties and biological function. The foremost classes of animal glycans include glycosaminoglycans (GAGs) that, with the allowance of hyaluronic acid, occur as proteoglycans and other conjugates such as glycoproteins and glycolipids. Glycans can mediate a wide range of biological developments by virtue of their physical properties, such as charge, molecular conformation, mass or gel-forming ability, and their biochemical function is indomitable by their nanoscale organization. On the other hand, several of the more detailed functions of glycans involve recognition by glycan-binding proteins (GBPs), such as lectins and GAG-binding proteins. In nature, all cells and various macromolecules carry a set of covalently linked glycans. The existence of glycans at the cell surface and in the ECM, place them in optimal station for facilitating a range of processes principal cell–cell, cell–matrix, and cell–molecule interactions, not only within an organism, but also between different organisms. Inspired by their biological roles, different biomimetic materials have been designed using native, modified, and synthetic glycans as building blocks [11].

3. **Design of glycan-based delivery systems**

Glycan-based biomaterials, from more unassuming oligosaccharides to more complex polysaccharides, can be engineered with exclusive properties and distinct arrangements, being predominantly engaging for the scheme of innovative drug-delivery systems. In these presentations, glycans from animal, nonanimal, and synthetic origins have been used, often chemically altered to accomplish detailed and consistent physicochemical properties and bioactivity [12]. To meet different needs, glycan based biomaterials have been administered into innumerable shapes, comprising micelles, nano/microparticles, hydrogels, nano/micro-fibers, and porous 3D scaffolds.

The design of glycan-based drug-delivery systems exploits unlike properties of this extremely diverse family of natural compounds. Provisional on the type of carbohydrate, some key properties may embrace (i) gel-forming facility, frequently used in the advance of matrix-type drug carriers; (ii) hydrophilic nature, which can be reconnoitred to enrich the circulatory half-lives of diverse types of drugs; (iii) polyelectrolyte nature, to encourage bottom up nano-assembly and/or complexation between glycans and drugs of opposite charge via electrostatic interactions; (iv) bioadhesiveness, recurrently subjugated as a means to increase drug retaining at certain localities, namely at mucosal surfaces;
and (v) affinity for GBPs, frequently engaged in the strategy of targeted carriers, such as glycan-decorated particles. There are also sugar-based compounds with very precise properties [13]. This is the case of cyclodextrins, a family of cyclic oligosaccharides made up of glucose monomers bound organised in a ring. Given the exceptional nature divulged by their structure, where the interior is substantially less hydrophilic than the exterior, cyclodextrins are able to form host–guest complexes with hydrophobic molecules, improving their solubility, physical chemical stability, and bioavailability. As such, these compounds have newly found a large number of solicitations in the drug-delivery field. Hydrogel-based matrix-type drug carriers have been gaining accumulative acceptance as ECM mimics for regenerative medicine and tissue engineering. In the ECM, gel-forming glycans provide hydration, structural stability, and selective permeability [14]. They are also elaborate in explicit, noncovalent binding of several endogenous molecules.

4. Hyaluronic acid

Hyaluronic acid (HA) is a natural, linear, endogenous polysaccharide that plays imperative physiological and biological roles in the human body. Currently, among biopolymers, HA is emergent as an alluring starting material for hydrogels proposal due to its biocompatibility, native biofunctionality, biodegradability, non-immunogenicity, and versatility. Since HA is not able to form gels alone, chemical adaptations, covalent crosslinking, and gelling agents are constantly desired in order to acquire HA-based hydrogels. Therefore, in the last decade, unlike approaches for the design of physical and chemical HA hydrogels have been advanced, such as click chemistry reactions, enzymatic and disulfide crosslinking, supramolecular assembly via inclusion complexation, and so on. HA-based hydrogels turn out to be adaptable platforms, extending from static to smart and stimuli-responsive systems, and for these reasons, they are extensively probed for biomedical applications like drug delivery, tissue engineering, regenerative medicine, cell therapy, and diagnostics. Additionally, the overexpression of HA receptors on many tumor cells makes these platforms favourable drug delivery systems for targeted cancer therapy. The aim of the present chapter is to highlight and confer recent improvements made in the last years on the design of chemical and physical HA-based hydrogels and their solicitation for biomedical purposes, in precise, drug delivery. Prominent devotion is given to HA hydrogel-based drug delivery systems for targeted therapy of cancer and osteoarthritis [15].
5. Keratin

Keratin derives from the Greek word “kera” which means a horn. In the 1950s, the word keratin first looked in the literature to define a substantial made up of hard tissues. In 1905, a United States patent was allotted labelling the process of keratin extraction from animal hooves with the help of lime. Since then, much research-based methods have been advanced with the aim of extracting keratin using primarily oxidative and reductive methodologies [16]. Primarily, these skills were pragmatic to extract keratin from animal-based sources such as horns, hooves, chicken feathers, and finally human hairs. These keratin-rich sources are challenging to vitiate as the polypeptide in their edifice is closely packed in $\alpha$-helix ($\alpha$-keratin) or $\beta$-sheet ($\beta$-keratin) into supercoiled chains which are toughly stabilized by numerous hydrogen bonds and hydrophobic interactions, in adding to the disulfide bonds, hooves, and horns [17].

In nature, the chicken feather is conceivably the greatest profuse and easily existing keratinous biopolymer. A keratin-based chicken feather from butchery accounts for more than 5 million tons per year global in the form of waste material [18]. Apart from its insignificant custom in low-grade products such as glue, corrugated paper, cardboard, animal feed, fertilizers, etc., the landfill disposal of poultry feather poses a substantial ecological and ecological threat. On the other hand, from the economic and ecological point of outlook, it is also anticipated to create an operative practice for the solicitation of such abandoned natural resource. The existence of multifunctional groups in keratin, such as disulfide, amino, thiol, phenolic, and carboxylic, makes it reactive under appropriate reaction situations. In a falling atmosphere, the amino and some of the further groups declared above in the keratin make its surface positive, and thus solubilization takes place. With its exceptional properties of biodegradability and nontoxic nature, keratin is amid the adaptable biopolymers that can be improved and advanced into several products of interests. Thus, a prominent amount of evidence on the features and hydrolysis of keratin has developed existing where intractable keratinous wastes are renewed into respected products [19]. The awareness on keratin-rich litters has been toughly increased and their use in cosmetics or in medicines to enrich drug delivery, and production of biodegradable films, are amid the principal and emergent biotechnological and biomedical applications [20].

In recent years, the emergent research comforts in the advance of keratin-based biomaterials are principally due to the exclusive properties of keratin that play a precarious role in the fabrication practice. Over the past few decades, exclusive physiochemical and biological characteristics of keratin have been emergent as factors for research based on biomaterials. To date, adequately of systematic work has been done and available by some experts on the advance and depiction of keratin and keratin-based
novel products, for instance, keratin-based composites/blends, (hydro)-gels, thin films, nano- and microparticles, and 3-D scaffolds are of supreme prominence. In various cases, the aforesaid novel keratin-based constituents are publicised to retain multifunctional faces along with exceptional compatibility sorts. Newly, we have revealed novel enzyme-based approaches for modulating the physiochemical, thermomechanical, and biological features of keratin in order to advance keratin-based bio-composite materials that have applicable structures for their probable solicitation of interest [21]. Later on, lactase was engaged as a green catalyst to advance natural phenol embedded keratin-EC-based biocomposites via the surface dipping and fusion technique. This work verified that the range of various natural phenols that Stimuli Responsive Polymeric Nanocarriers for Drug Delivery uses embraces caffeic acid, gallic acid, p-4-hydroxybenzoic acid, and thymol could exclusively regulate the antibacterial probable of these newly established novel bio-composites. Figure 2, exemplifies a graphical depiction of advance and unique features of phenol-g-keratin-EC-based bio-composites. Correspondingly, Verma and co-workers had reported construction, depiction, and biocompatibility of human hair-based keratin scaffolds for in vitro tissue engineering solicitations [22].

![Figure 2 Development and novel characteristics of Phenol-g-Keratin-EC-based bio-composites.](image)

6. Cellulose

Cellulose being the first plentiful biopolymers in nature has many enthralling properties, counting low-cost, good biodegradability, and exceptional biocompatibility, which made
cellulose a real probable substantial to generate nano-drug delivery systems (nano-DDS). In recent decades, cellulose has been expansively explored due to its approving properties, such as hydrophilicity, low-cost, biodegradability, biocompatibility, and non-toxicity, which marks it a good feedstock for the synthesis of biocompatible hydrogels. The plentiful hydrophilic functional groups (such as hydroxyl, carboxyl, and aldehyde groups) in the backbone of cellulose and its spinoffs can be used to concoct hydrogels easily with attractive structures and properties, prominent to burgeoning research interest in biomedical requests. By probing the research literatures over last decade, an assortment presented studies on cellulose based nano-DDS were brief and alienated into prodrugs, prodrug nanoparticles, solid or derived nanoparticles, amphiphilic copolymer nanoparticles, and polyelectrolyte complex nanoparticles [23].

Many types of cellulose-based nano-DDS can confirm proficient encapsulation of various drugs and then overawed the free drug molecule flaws. Among all the process designated, cellulose based amphiphilic nanoparticles are most recurrently used. These formulations have the higher drug loading capability, a simple and stretchy way to realise multifunctional. Apart from hydrophilic or hydrophobic reform, cellulose or its spinoffs can form nanoparticles with diverse small molecules and macromolecules, foremost to a large spectrum of cellulose-based nano-DDS and so long as some startling benefits. Thorough physicochemical portrayal and reflective indulgent of interactions of the cellulose-based nano-DDS with cells and tissues is vital. Furthermore, studies near technics constraint optimization and scale up from the laboratory to production level should be assumed. The advance of intravenous and orally pertinent cellulose-based nano-DDS will be an imperative research area, and these systems will have more viable status in the market [24].

Cellulose-based hydrogels are resultant from natural sources which are biodegradable and low-immunologic. These hydrogels are produced in four different ways: those acquired directly from native cellulose, those imitative from cellulose derivatives (methyl cellulose, carboxymethyl cellulose, hydroxy methyl cellulose, etc.), those acquired with other polymers as a fused, and lastly those gained from cellulose-inorganic hybrids. Cellulose hydrogels and its spinoffs have many desired properties such as high water retaining capacity, high crystallinity, fine fiber network, easy formability, and high tensile strength. In addition, some cellulose spinoffs display able performance against physiological variables such as pH and ionic strength. Cellulose-based hydrogels have gains such as better biocompatibility, less latent toxicity, and lower cost than the utmost synthetic polymer hydrogels. Because of these benefits, cellulose-based hydrogels are desired to be used in industrial pharmaceutics and biomedical fields [25].
7. Chitosan

Chitosan is attained from the deacetylation of chitin, and it is a copolymer of \(N\)-acetylglucosamine and \(d\)-glucosamine. Distinct chitin, chitosan is soluble, and its properties make it easy to handle and accomplish [26]. Both chitin and chitosan have been extensively used in biomedical solicitations with exact emphasis on drug delivery potentialities. Chitin has exposed highly hydrophobic properties caused by the \(N\)-acetylglucosamine polymeric structure which makes it a hard material, but it also has admirable electric properties which may be pragmatic to tissues requiring electrical conductance. Besides being a soluble polymer, chitosan presents novel features such as high biodegradability and biocompatibility, nonantigenicity, good adsorption properties, nontoxicity, and bio-functionality. The above stated characteristics of chitosan play a vital role in emergent smart therapeutic and health-related drug delivery systems. Likewise, it can be pragmatic to engineer novel carriers combining the polymer with carbon nanotubes, which increase the electrical conductivity of the scaffold [27].

8. Polyhydroxyalkanoates (PHAs)

Polymers that are formed by biological systems such as plants, animals, or microorganisms through metabolic-based engineering reactions are called natural polymers. Instances of biopolymers comprise carbohydrates, for example, cellulose and starch, proteins, for example, keratin and enzymes, and polyhydroxyalkanoates (PHAs), for example, poly-(3-hydroxybutyrate) \([P(3HB)]\) [28]. A wider spectrum of such materials has been categorized consequently as natural or synthetic based on their nature of origin. The structure of a biopolymer distresses its functional characteristics where the functional capability is frequently reliant on the crystalline and amorphous nature of the materials. For example, cellulose or poly(\(\beta\)-d-glucose) is a structural polymer whose properties arise in part from its crystalline nature. Nevertheless, physiochemical and biological dealings can transform it into a beneficial structural material for many probable solicitations. Also, chemically revised cellulosics, for example, ethyl cellulose and cellulose acetate, are found in a wide range of presentations. Modified cellulose is used in the manufacture of paint, plaster, adhesives, cosmetics, and pharmaceutical film coating and numerous other products. A family of compounds known as PHAs has acknowledged much courtesy as bio-sustainable materials because they are formed more certainly in extent by fermentation of carbon–rich substrates using microorganisms, particularly bacteria. Among the utmost likely and well characterized biopolymers, \(P(3HB)\) is of exact interest for the preparation of bio-based composite materials. There have been more than 150 monomers notorious as elements of PHAs [29]. The unhinged
nutritional supply origins the bacteria to collect PHAs in the form of granules as internal energy storage, as shown in figure 3.

![PHA granules](image)

**Figure 3:** (A)-PHA granules, (B)- Schematic representation of PHA granules

## 9. Nucleic acid based nanodelivery systems

The enhanced appreciative of the genetic roots of plentiful diseases going hand in hand with the achievement of the human genome project opened the door for the discovery of novel therapeutics precisely curbing the expression of disease-relevant genes. Largely, this therapeutics can be considered into viral and non-viral formulations. The non-viral ones offering the overlook of eluding oncogenic risk and of dealing hypothetically larger payloads is either plasmid DNA (pDNA) encoding for therapeutic proteins such as GLP-1 or insulin and in case of DNA vaccines for antigens or RNA-based drugs with antisense oligonucleotides, short interfering RNA, microRNA, messenger RNA, and Aptamer. In disparity to all other drugs they can edit genes curing accordingly genetic defects. Additionally, they can be used to shut off assured gene expression. In the case of certain gastrointestinal diseases, such as inflammatory bowel disease (IBD) and colon cancer, where current drug cures are scant such gene-based therapeutics may require major clinical benefits [30].

Gene therapy with RNA and pDNA-based drugs is inadequate by poor enzymatic stability and poor cellular permeation. The provision of nucleic acids, in precise by the oral route, rests a major hurdle. These will emphasize on the barriers to the oral delivery of nucleic acids and the plans, in exact formulation strategies, which have been advanced to daze these barriers. Due to their very low oral bioavailability, the most noticeable and most explored biomedical claims for their oral delivery are related to the local treatment of inflammatory bowel diseases and colorectal cancers. Preclinical data but not yet clinical studies sustenance the potential use of the oral route for the local delivery of formulated nucleic acid-based drugs [31].
10. Lipid based nanodelivery systems

Lipids are a large class of materials that embraces fatty acids, glycerides, phospholipids, sphingolipids, waxes, and sterols. These compounds are frequently insoluble in water, or Design and preparation of biomimetic and bioinspired materials amphiphilic, and are recognised by their fatty-acid alignment, melting point, hydrophilic–lipophilic balance, and solubility in organic solvents. Lipid-based systems have expanded much interest in the modern years for drug-delivery resolves primarily due to their facility to expand the solubility and bioavailability of drugs with poor water solubility. Nevertheless, lipid-based systems have also verified superior ability for hydrophilic drugs, tailoring the release profile of the active contents in a biofunctional manner [32]. The most substantial dosage forms are liposomes, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), and self-emulsifying drug-delivery systems (SEDDS).

Liposomes are spherical vesicles poised of bilayers of phospholipids, cholesterol, and/or other lipids. Lecithin, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, and phosphatidylserine are the chiefly used phospholipids. They can be categorized bestowing to their lamellarity as uni, oligo, and multilamellar, or by size as small, midway, and large. Due to its structure, they permit the assimilation of hydrophilic drugs in the aqueous core, and lipophilic drugs within the lipid bilayer as shown in figure 4. Retaining higher core, unilamellar liposomes are desired for encapsulation of hydrophilic drugs, while multilamellar liposomes are specifically used to encapsulate hydrophobic drugs due to the higher lipid content. Reliant on the number and composition of the bilayers and the incidence of coating, it is probable to acquire systems with modified release characteristics. Besides the marketed formulations, liposomes have been advised for administration of numerous drugs, comprising peptides and therapeutic proteins, as well as for gene therapy). Stealth liposomes like Doxil/Caelyx, Novantrone, or Lipoplatin are commercially existing examples of second-generation liposomes, surface-decorated with PEG moieties, ensuing in advance of blood circulation time and the therapeutic efficacy of many drugs through the evading of opsonisation, that is, exclusion by immune cells, and drip from reticuloendothelial system [33].

11. SLNs and NLC

Lipid nanoparticles mostly embrace two types of structures, SLN and NLC. They contain a solid lipid matrix, usually vastly refined triacylglycerols, complex acylglycerol mixtures, and even waxes, at room and body temperatures, dispersed in aqueous solution and stabilized with a layer of emulsifier agent, usually phospholipids. Lipid nanoparticles began as an substitute to liposomes because of the superior stability in biological fluids.
They are colloidal carriers made of nontoxic [34], biodegradable and well-tolerated solid lipids dispersed either in water or in an aqueous surfactant solution. The lipid composition can delay degradation by impeding the quay of enzyme complexes, qualifying their probable for controlled drug delivery. Additional benefits of SLN are their particulate nature, facility to integrate both hydrophilic and hydrophobic drugs, the evading of organic solvents in the production procedures and the prospect to produce vastly concentrated lipid suspensions, lower cytotoxicity, and scale-up probability. Hydrophobic anticancer drugs such as camptothecin, anti-rheumatics such as methotrexate, or immune-suppressants as cyclosporine have been encapsulated into SLN for modulating there in vivo biodistribution and target drugs for their local of action. SLNs are also able to compress biopharmaceutical drugs with high aqueous solubility, retentive their structure after encapsulation and even freeze-drying. Therapeutic proteins or genetic material are presently formulated into solid lipid matrix, ensuing in biocompatible and environment-friendly conditions to alleviate those biological [35].

A second generation of lipid nanoparticles is the so-called NLC. These particles are primed not from a solid lipid but from a composite of solid and liquid (oils) lipids, which must be solid at least at 40°C. The foremost variance amid SLN and NLC is that the latter are articulated by nano-structuring the lipid matrix to increase drug loading and avoid drug expulsion. Using spatially diverse lipids leads to larger distances between the fatty acid chains of the acylglycerols and broad limitations in the crystal, on condition that more room to lodge drugs. The utmost drug loads could be accomplished by mixing solid lipids with small amounts of liquid lipids. Several drugs show a higher solubility in oils than in solid lipids, thus they can be dissolved in the oil and still be dwindling from degradation by the adjacent solid lipids [36].

![Figure 4 Schematic representation of (A)-liposome, (B)-SLN and (C)-NLC.](image-url)
12. Peptide based nanodelivery systems

Peptides offer numerous benefits as building blocks for the intention of drug-delivery systems. They are endogenous molecules, which diminishes the risk of contrary effects; are poised of nonpolar, polar, or exciting amino acids, consenting a assured level of expectation of the self-assembly properties complete the meticulous medley of the peptide structure; may range from short to long and more stretchy chains assisting the assembly of structural diverse schedules, from solid crystals to soft disorderly materials; and are rather easy to synthesize and in some cases (short peptides) are commercially presented at practical prices. Moreover, the significant physicochemical properties of peptides enable them to initiate responsive materials to impetus such as temperature, pH, or the presence of specific molecules [37].

Short peptides have been vastly used in the tuition of both crystalline and of soft materials. Diphenylalanine occurred as probably the utmost adaptable, with presentation in nanoelectronics, tissue engineering, or as a model to inspect the molecular mechanisms of protein aggregation in amyloidogenisis. Numerous hydrophobic dipeptides, comprising diphenylalanine, are capable to create microporous crystals fashioned by hydrogen bond-induced head-to tail rally of dipeptides into helical arrangements. The crystal frameworks classically encompass 1D channel with a diameter of 3–10 Å. They were tested as adsorbents of numerous gases such as Xe, CO2, CH4, H2, Ar, N2, and O2) and may find exciting biomedical presentation in the delivery of gasotransmitter molecules. Dipeptides were also fused in hybrid metal–organic materials performance exciting adsorption properties. Oligopeptides may self-assemble into numerous dissimilar architectures with perhaps even higher biomedical interest than microporous crystals, such as tubes, rods, fibrils, spheres, vesicles, and gels. Nanovesicular structures have been extremely probed for the delivery of hydrophobic drugs [38]. Also 3D cultures of nerve cells, endothelial cells, and chondrocytes were previously fruitfully shown in decidedly hydrated short-peptides-based scaffolds, like, for specimen, from the simple amphiphilic building blocks involving of dipeptides linked to fluorenlymethoxycarbonyl (Fmoc, roughly used as a protective group in peptide chemistry). The unification of small organic moieties or of unnatural amino acids has been recurrently used to normalise the physicochemical properties and to surge the proteolytic and thermal stability of these peptides. The properties of the final material are also overseen by the experimental disorders through the self-assembly. For request, a peptide amphiphile (PA) hydrogel produced by two diverse triggers, HCl and CaCl2, ensuing in gels with parallel structure but bizarrely different viscoelastic properties. Whereas CaCl2 produced a stronger gel with tighter inter- and intrafibril crosslinks, HCl encouraged a more flexible structure capable of hastily improving its shape after
distortion. It is still a major encounter to design a novel peptide-based material with 
determined properties. Several design approaches are being advanced, mainly relating 
either the production of PAs or the presentation of the familiarity gained from protein 
secondary structural subjects, such as α-helix and β sheet. Though a greater number of 
revisions have concentrated on peptides folding into β-sheets, probably as a result of the 
high research motion on amyloid-like structures, α-helical folding has newly been 
unloading increasing attention [39]. This fact could be linked to the exact set of rules that 
have been customary for the assembly of α-helices that can lead to a rational molecular 
design.

13. Bacteria/ Viral-based delivery systems

Bacterial cells enjoy exclusive characteristics that make them ideal contestants for cancer 
therapy. They can lance deep into remote tumor regions and colonize hypoxic and 
necrotic regions. They also expose evidence about the state of tumors and the ability of 
treatment because they are superficially noticeable. Some forms of bacteria such as 
Bacillus, Bifidobacterium sp., Listeria sp., Salmonella sp., Mycobacterium, and 
Clostridium are known to act as anticancer agents. Bacteria species can be added altered 
genetically to rally their properties and exploited as vehicles to deliver drugs, proteins, 
enzymes and genes for the management of cancer, with various cases reaching several 
phases of clinical trials, hence assembly them superb carriers for the production and 
targeted delivery of therapeutic cargos into cancer tissues. The exciting approach to 
genetically engineer bacteria with a drug release switch was used as a way to 
concurrently control the bacteria’s population growth and simplify drug delivery [40].
Bacterial ghosts are the utmost mutual form of cellular cloaks and are distinct as substrates imitative from Gram-negative bacteria lacking of genetic material. They are produced by controlled expression of the cloned lysis gene E from bacteriophage species. The use of bacterial ghosts in its place of live bacterial cells for drug delivery has some further benefits, so they have fascinated much consideration over the years. BGs do not inhabit the vibrant organs of the body, later reducing the risk of undesirable side effects; they are vastly stable and can realm their surface structures, thus retaining their immunomodulation capacities. Microbots Bacteria can also be used concurrently with nanoparticles to deliver therapeutic cargos into cells. Bacteria carry the drug on their surface conjugated to nanoparticles; hence the bacteria do not require genetic engineering for the delivery process. This practise takes lead of the hostile properties of bacteria, and this type of bacteria are known as microbots, which have the probable to selectively colonize the hypoxic areas of tumors that cannot be cured by predictable chemotherapeutic drugs. α-Helix is a key secondary structure of natural proteins that entails of a peptide chain coiled into a right-handed spiral conformation and stabilized by hydrogen bonds amid the N-H and the C=O groups in the backbone [41]. Methionine, alanine, leucine, glutamate, and lysine have distinct proclivity to be part of α-helix edifices while proline and glycine have poor helix-forming proclivities. A principally

Figure 5 Examples of potential biological vehicles tolerated naturally in selected organs.
profuse α-helix-based structural motif is the coiled coil, in which the α-helix is regularly considered by a seven residue echoing unit of flashing hydrophobic and hydrophilic residues, often signified as \((abcdefg)n\).

Coiled coils have been used for drug delivery isolated or merged in liposomes and for the intention of supramolecular materials. Coiled coils display an inner hydrophobic core that can be discovered to convey hydrophobic drugs. The probable of loading cisplatin, a hydrophobic chemotherapeutic drug, into a right-handed coiled coil (RHCC). RHCC encompassing the drug was able to bind and enter cells in vitro. Unsurprisingly stirring coiled coils, such as the leucine zipper, led to the gratitude of classification necessities for the congress of these structures [42].

Moreover, temperature receptive materials were previously designed Banwell et al., [41] by trading amino acids at this same fringe region; in one case they assimilated alanine to stimulate hydrophobic interactions between fibrils and in alternative by glutamine to adoptive hydrogen bonding. In both cases physical hydrogels were acquired, with the exactitude that glutamine-based gels were bent at low temperature although alanine-based gels were accomplished at high temperature. Thermo-responsive coiled-coil peptides were also inserted in liposome membranes to allow greater control over the release of fenced compounds in retort to temperature. In a recent work planned a supercharged coiled coil structure bearing numerous arginine residues that was magnificently complexed with plasmid DNA and encapsulated it in a liposome for gene therapy [43].

14. β-Sheet

β-Sheet is the further form of secondary edifice present in proteins and comprises of β-strands allied edgewise by backbone hydrogen bonds and arranged in a parallel or antiparallel fashion. Much like the α-helix, β-sheets can be made amphiphilic to simplify the design of design guidelines. Since in β-sheets, the side chains consecutively stick out of the plan in opposite directions, the HPHPHP outline forms β-sheets with a hydrophilic side and a hydrophobic side, which instinctively self-assemble. One of such rallies (RADA16, where R stands for arginine, A for alanine, and D for aspartic acid) is now promoted, mostly for exploration resolves, below the commercial name Pura Matrix. Numerous studies have engaged these hydrogels for cell culture, signifying it’s impending for tissue engineering presentations [44]. It was also revealed that RADA16 is seemly for the slow delivery of proteins; the releasing kinetics is reliant on the size and charge of the macromolecules but it is also a function of the peptide density in the gel. By hosting a phenylalanine residue on the RADA16 structure, purposefully fashioned a motif for interaction with hydrophobic drugs. This group probed two peptide systems, RADAFI and RADAFII, the hydrogels were revealed to ensnare molecules comprising the phenyl
group, ostensibly by $\pi-\pi$ interaction, provided that another ground confirmation of the probable of these materials for drug delivery.

15. Peptide amphiphiles

Peptide amphiphiles (PAs) are double character molecules whose self-assembling mechanism is similar to that of phospholipids in cell membranes. To intention a PA, a hydrophobic important domain usually in the form of a polymer or alkyl chain, or less habitually, a structure of nonpolar amino acids-linked to hydrophilic peptides. When placed in aqueous environment such amphipathic character molecules tend to accumulate into supramolecular architectures such as spherical or cylindrical micelles. The facility to encapsulate hydrophilic molecules has previously been revealed by van Hell et al. [45] who testified the design of numerous PAs, which self-assemble into vesicles. In addition to on condition that a proficient carrier situation, these systems also extant the improvement of consenting a fine control of the properties of the muster surface by judicious selection of combining amino acids. The adaptability by combining lysines in the plan of a PA molecule to confer pH-responsiveness. The PAs self-assembled into micelle, ensnaring DOX, an antineoplastic drug that is released when placed in acidic environments due to electrostatic repulsions between the protonated lysine molecules. Other effective drug carriers based on PAs have been fashioned and a composing of carriers based on peptide self-assemble.

16. Virus-inspired drug delivery systems

Viruses are small infectious microorganisms entailing of nucleic acid molecules in a protein coat. They have been freshly used as vehicles for targeted delivery as they have the facility to transferal their genes into the host cells for imitation. Conjoining targeted viral vectors with drugs crafts an elevated anticancer effect since it synergizes the sympathetic aspects of both constituents. This type of combinatorial system epitomises an inventive slant for the design of tumor-targeted nanoparticles. Instances of viruses frequently used as viral vector systems comprise adenoviruses, adeno-associated viruses and retroviruses [46]. It was revealed in a revision that nanoparticles could be explicitly conjugated to diverse adenovirus capsid proteins and targeted to tumor cells. It was also perceived that these NP-labeled Ad vectors revealed the same level of targeting and infection proficiency to tumor cells as the unlabeled Ad vectors. For this purpose, it was resolved that Ad vectors can serve as a platform for the choosy self-assembly and targeted delivery of NPs to the target cells. By relating nanotechnology with gene concepts, it is probable to intention a multifunctional nanoscale device for cancer treatment. In alternative study, hyperthermia-inducing gold nanoparticles were involved
to adenoviral vectors via m-covalent conjugation. These nanoparticles were engineered to target a tumor-associated carcino-embryonic antigen without mutable the infectivity of the viral vectors. There is a thorough discussion on the attractive virus-inspired delivery systems, which are reflected very innovative.

Virus-like particles (VLPs) are exceedingly orbicular self-assembled capsids consequent from viruses. VLPs are made of vacant shells lacking of genetic material and they are non-infectious. They are, nevertheless, adept of arriving target cells and can be used to deliver therapeutic cargoes such as peptides, antigens, and anticancer drugs. VLPs are anatomically stable and accepting to employment; their production development can be concluded at a low cost, thus well allocation as a carrier for drug molecules or building blocks for novel nanomaterials. In a study, paclitaxel was conjugated to VLPs that were derived from the bacteriophage MS2; paclitaxel did not conciliation viral capsid functionality [47].

Virosomes are a class of viruses that comprise a cohesive glycoprotein with a vacant inner compartment and they are also identified as re-formed viral particles. Virosomes are often created by solubilizing influenza virus with detergent and then reconstituting it with two influenza envelope glycoproteins: neuraminidase and haemagglutinin. These glycoproteins are liable for the structural homogeneity and stability, targeting, receptor-mediated endocytosis and endosomal escape after endocytosis of virosomes. One foremost benefit of virosomes as carrier systems is their talent to protect pharmaceutically active substances from proteolytic degradation and low pH within endosomes, submissive the satisfied to stay intact when attainment the cytoplasm. Freshly, an erythro-magneto-haemagglutinin virosome was premeditated for the delivery of the therapeutic formulation of decitabine. It was detected that this system explicitly elated the drug into tumor tissues and convinced tumor mass reduction in xeno-graft models of prostate cancer at a lower concentration than the therapeutic dose prerequisite by the free drug [48].

Virus-mimicking particles have over modest and conventional delivery carriers in terms of drug retention and targeting. Viruses are filamentous, and as such, filomicelles were synthesized to mimic the morphological features of viruses [49]. Filomicelles are serene of self-assembling amphiphilic block copolymers and can excellently evade the reticuloendothelial system, principal to a considerably longer blood circulation time in vivo. Earlier research reports perceived that paclitaxel loaded in filomicelles shrank tumors more excellently than the drug solution. The shape and flexibility of filomicelles may also impact their circulation and targeting competency as a capable as drug delivery carrier, while mechanisms for in vivo efficacy are being inspected. Virus-mimetic nanogels that are pH-sensitive have been synthesized. They mimic the structural and
functional characteristics of viruses and involve of a hydrophobic core and two layers of hydrophilic shells with tumor-targeting ligands. In a study, DOX was elegantly loaded into the hydrophobic core of a virus-based expedient. To mimic the capsid-like structure of viruses, PEG was crosslinked to the core polymer, and bovine serum albumin was assured to the other end of PEG. These formed particles were pH-sensitive as such a pH reduction from a physiological to an endosomal level would convince alterable swelling and a particle size increase of the nanogels. The conversion aided the endosomal escape and release of DOX into the cytosol. Once tumor cells were executed by DOX and split, nanogels would move to neighbouring cells and repeat the cycle, exciting the infection replication of viruses. The talent of pH-sensitive nanogels to escape from endosomes and unremittingly infect adjacent cells is also capable. The above approaches are in infant stages and their aptitudes and mechanisms entail added explication, which determines that radical bioengineering afar simple surface reform of viruses into synthetic provision carriers and uses of these virus-mimicking particles in targeted drug delivery would absolutely extend the clinical choices of cancer therapy in the near prospect [50].

17. Mammalian cell-based drug delivery systems

Mammalian cell-based delivery systems have assembled accumulative devotion, due primarily to their facility to sham many natural properties exposed by their source cells. By merging synthetic NPs with changed cell types such as leukocytes, platelets, and red blood cells, it was potential to cultivate a range of cell membrane-cloaked nanosystems with exceptional features and functions. In a nut shell, living cells not only offer rousing probable in novel drug delivery, but also assist a better indulgent of natural tools upon drug admin [51].

18. Erythrocytes (RBCs)

Red blood cells or erythrocytes are springy and oval biconcave disks with an average diameter of 7–8 μm. They exist as the most profuse cells in mammals, and are the primary transporter of oxygen in human body. RBCs retain high biocompatibility and ample biodegradability without crafting toxic products in vivo, and when equated to synthetic carriers, they exhibit unique features such as sustained circulatory half-life (∼120 d in humans and ∼40 d in mice) and the facility to exchange certain prodrugs due to enzymatic existence, thus interim as active transporters. In addition, RBCs have vacant volume for drug encapsulation. They also afford ample coating space to bestow diverse carrier functionalities. Some practices can easily alter RBCs without varying their biological properties [52].
RBCs are acquired from altered mammalian species, and the isolated blood is collected into heparinized tubes by venipuncture formerly being used as carriers. Loading RBCs with the chosen drug molecules can be done during several key means counting electroporation, molecule endocytosis, and hypo-osmotic swelling, which is then monitored by resealing and bestowing cell-penetrating peptides in most cases. The modern design may also employ RBC membranes as a coating for polymer nanoparticles, which has been attested to be popular and hopeful. RBCs will advanced an emergent approach for targeted delivery of anticancer drugs in the near imminent. In a study, Aryal et al. [53] advanced RBC membrane cloaked polymeric nanoparticles (RBCm-cloaked NPs) to deliver DOX. This system seemingly delivered a pooled benefit of both a long circulation epoch and controlled drug release ascribed to the red blood cells and polymeric particles, separately. Two approaches to load DOX into RBCm-cloaked NPs were paralleled in this study, and the results revealed that RBCm-cloaked NPs could potentiate great assurance as a drug-delivery platform in handling diseases such as blood cancer. In alternative study, a RBC-based micromotor was considered to load an imaging agent, CdTe quantum dot (QD), and DOX, to exhibit the coupling of both therapeutic and imaging modalities within a single vehicle. The multi-cargo-loaded, RBC-based micromotors were primed by concurrently loading water-soluble CdTe QD nanocrystals, DOX and iron oxide magnetic nanoparticles into RBCs using a hypotonic dilution based encapsulation method. The outcomes of this study specified that RBC micromotors were adept of concurrently carrying multiple functional cargos with a minimal injurious effect on its dynamic propulsion behaviour and compatibility, which would consequently expand drug delivery efficacy and disease monitoring. It was determined from this revision that a RBC micromotor could offer a novel platform for concurrently imaging a disease, providing an agent and observing therapeutic retort in future theranostic presentations. Adaptation of RBCs thru the drug loading practice is foreseeable; nevertheless, this strategy may hasten the abstraction of delivery carriers by reticuloendothelial cells. Moreover, unlike constraints such as the source of blood, the apparatus used, and the formulation practice may subsidise to the rapid outflow of specific drug encapsulation after preparation or admin. Hence arduous precautions are prerequisite therefore to accomplish optimal handling and treating of the erythrocyte carriers.

19. Immune cells

Immune cells are a group of cells that elicit retorts against foreign elements in order to protect the body against diseases; these cells hereafter cooperatively form the immune system. There are diverse types of immune cells such as lymphocytes, natural killer cells,
phagocytes, and neutrophils. Leukocytes, also known as white blood cells (WBCs), are a part of the immune system and play a substantial role in suppressing inflammation, infection, and several disease conditions. WBCs have a shorter circulation time (up to 20 days) than RBCs, but they are still smart for drug delivery presentations, because of their specific features, such as increased cellular interactions and substantial tissue penetration capabilities, in exact across physiological barriers [54]. Additionally, WBCs tend to transport, migrate near inflammatory sites and adhere to endothelial wall tissues with tumor cells, aspects highly seemly and capable for novel drug delivery in cancer treatment. Macrophages are one type of WBCs principally designed in bone marrow and derived from monocytes that separate concluded promonocytes from monoblasts. The practice of phagocytosis by macrophages can overcome and digest cellular debris, microbes, cancer cells and other dangerous substances that entered human body. Macrophages have a distinctive facility to differentiate between spiteful and benign cells, though they someway show constraint in individual between unlike types of bacteria, viruses and other foreign constituents. They also retain a homing property and can transfer to tumor sites across endothelial barriers in retort to cytokine excretion from diseased tissues. The conception of macrophage phagocytosis in close conjunction with improvements in nanotechnology has newly been used to combat diseases where therapeutic nanoparticles are being loaded ex vivo into macrophages. Cell-based delivery systems using macrophages are valuable since the intracellular cargo of the cells would endure dormant and harmless to its host deprived of premature release until reaching tumor cells and carrying a strong drug dose. As such, macrophages would act as Trojan horses to carry drug loading nanoparticles, pass through barriers, and offload them into brain tumor sites [55].

20. Stem cells

Stems cells have also appeared as a impending therapeutic aspirant in cancer therapy in modern years, chiefly for gene therapy. Stem cells organised with leukocytes parade intrinsic tropism on inflammatory and tumor sites; later it is imaginable to exploit genetic engineering as well as tumor tropism to convince stem cells to prompt therapeutic gene products that encode antitumor proteins. For example, the realisation in incorporating lipid and polymeric nanoparticles into non-transformed adult human mesenchymal stem cells (MSCs), and the outcomes publicized the capacity of MSC nanoparticles to drift to brain tumors without conciliation of their possibility. In alternative study, MSCs loaded with PLGA-DOX nanoparticles were used to treat pulmonary metastases. Exact targeting to tumors and carrier permeation were perceived; the homing and permeability properties of MSCs were not precious by drug loading, and their ability and knack to kill melanoma
21. Platelets

A platelet is a necessary element of the bloodstream and plays a key role in numerous physiologic and pathologic developments such as hemostasis and thrombosis by establishing the plugs that seal injured vessels and stop bleeding and conserving the reliability of blood circulation. Newly, the natural affinity of platelets for circulating tumor cells (CTCs) that are shed from the primary tumor into the bloodstream has drained great attention. The average lifespan of circulating platelets is 8 to 9 days, and hence could prominently expand the pharmacokinetics of intravenously injected therapeutics. Furthermore, transfused platelets retain the facility to migrate to the site of surgical wounds, where residual tumors may survive after surgery. This delivery approach took improvement of the empathy of platelets for cancer cells and the complex could excellently deliver to cancer cell membranes and initiate the extrinsic apoptosis indicating lane. Subsequently, it was digested after endocytosis and enriched amassing at the nuclei for initiation of the essential apoptosis pathway; hence a encouraging synergetic antitumor efficiency was accomplished. Lastly, the complex could added be revised to detect and exclude metastatic tumor cells, thus allotment great ability in cancer therapy [57].

22. Concluding remarks and future perspectives

Bioengineering of nanoparticles is a swiftly mounting field, with tremendous improvements in the last decade. Delightful improvement of the unambiguous delivery and translocation mechanisms espoused by pathogens and mammalian cells, the bioinspired nanoparticles have diverse functions, such as extended circulation, enriched amassing at infected sites, and reduced off-target effects in healthy tissues. Biological complexity affords desired functions to bioinspired nanoplatforms, which concurrently causes encounters for practice control, refining, scaling up production, and reproducible manufacturing in the research stage. On the basis of the quality-by-design principle, the advantage of minimalism should be monitored to expedite translation studies. Nanoparticles engineered by innumerable biomimetic slants, their structural features and molecular constituents are only unwell considered. Impending revisions are vital to expose details concerning the exact constituents as well as the dissemination,
 arrangement, and orientation of precise biomolecules on the surface of bioinspired nanoparticles, since these constraints are exceptionally essential for their in vivo fates and therapeutic efficacies. In this aspect, incipient expertise such as multiplexed protein analysis, proteomics, and imaging mass spectrometry can be used. Institution of the structure–property correlation will be favourable for streamlining or enhancing preparation processes of remaining biomimetic nanoparticles. This can also stimulate the intention and advance of more operative nanoplatforms. Subsequently, the usefulness and long-term safety concerns of newly bioengineered nanotherapies need to be established by comprehensive anti-infective studies. Similarly, mechanistic studies should be conducted to address molecular and cellular events controlling in vivo biopharmaceutical and pharmacokinetic profiles of biomimetic nanotherapies presently advanced. Other cutting-edge technologies, such as computational design, materials genome, and artificial intelligence, can be integrated to discover more effective and translational nanoparticles based on the bioengineering strategies. Despite the aforementioned challenges and restrictions of bioinspired nanotherapies for biomedical applications, we may expect that the biomimetic strategy-based nanomedicine field will afford novel therapeutics against infectious diseases in the near future.

In conclusion, with many promising suggestions developed in modern years where new drug delivery and imaging technologies are advanced, there is a positive position for bio-inspired nano-theranostics and its clinical rendition could be recognised in the near future to reform cancer therapy.

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